PATENTTI- JA REKISTERIHALLITUS
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Helsinki 11.11.2003

PCT/FI 03/00726

10/530024

01 APR 2005

E T U O I K E U S T O D I S T U S
P R I O R I T Y D O C U M E N T

REC'D 28 NOV 2003
WIPO PCT

Hakija Applicant	Karyon Oy Ab Ltd Helsinki
Patenttihakemus nro Patent application no	20021762
Tekemispäivä Filing date	03.10.2002
Kansainvälinen luokka International class	C07K
Keksinnön nimitys Title of invention	"Novel therapeutic substances and compositions" (Uusia terapeuttisia aineita ja valmisteita)

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Novel therapeutic substances and compositions

Field of the Invention

The present invention relates to tissue targeting agents comprising one or more targeting units and one or more effector units and to targeting units and to motifs that are the targeting units or form parts of the targeting units. Further, the present invention concerns pharmaceutical and diagnostic compositions comprising these targeting agents and/or targeting units, and the use of these targeting agents and/or targeting units as pharmaceuticals *in vitro* and/or *in vivo* and/or as diagnostic tools *in vivo* and/or *in vitro*. The invention relates also to the use of these targeting agents and/or targeting units for the preparation of pharmaceutical and/or diagnostic compositions and/or for the preparation of reagents to be used in diagnosis and/or research. Further, the invention relates to kits for diagnosing and/or treating cancer and/or metastases. Still further, the invention relates to methods of removing, selecting, sorting and/or enriching cells, and to materials and kits for those methods. This invention relates furthermore to targeting agents, units, motifs, or their structurally and/or functionally equivalent analogues for use in treatment and/or diagnosis of cancer.

Description of Related Art

Malignant tumors are one of the greatest health problems of man as well as animals, being one of the most common causes of death, also among young individuals. The available methods of treatment of cancer are quite limited, in spite of intensive research efforts during several decades. Although curative treatment (usually surgery in combination with chemothreapy and/or radiotherapy) is sometimes possible, malignant tumors (cancer) still are one of the most feared diseases of mankind, requiring a huge number of lives every year. In fact, curative treatment is rarely accomplished if the disease is not diagnosed early. In addition, certain tumor types can rarely, if ever, be treated curatively.

In essence, the treatment of cancer in a large proportion of cases is merely palliative or at best prolongs survival without providing a real cure of the disease. There are various reasons for this very undesirable situation but the most important one is clearly the fact that nearly all (if not all) treatment schedules (except surgery) are essentially or largely devoid of sufficient selectivity. Thus, the chemotherapeutic agents commonly used, such as alkylating agents, platinum compounds (e.g. cisplatin), bleomycin-type agents, other alkaloids and other cytostatic agents in general, do not act on the malignant cells of the tumors alone but are highly toxic to other cells as well, being usually especially toxic to rapidly dividing cell types, such as hematopoietic and epithelial cells.

In addition to the above mentioned complications, two further major problems plague the non-surgical treatment of malignant solid tumors. First, physiological barriers within tumors impede the delivery of therapeutics at effective concentrations to all cancer cells. Second, acquired drug resistance resulting from genetic and epigenetic mechanisms reduces the effectiveness of available drugs.

As a result of the largely non-selective action or (at best) limited selectivity of currently available anti-cancer drugs, curative treatment may be impossible using prior art drugs and treatments, since administration of doses large enough to cure the disease would have fatal consequences or too serious side effects to be tolerated. One reason for a fatal outcome with present-day treatments is bone marrow suppression, leading to erythropenia, leukopenia and/or thrombopenia. Hepatotoxicity, cardiotoxicity, nephrotoxicity, ototoxicity and other toxicities may also be dose-limiting as specialists in the field very well know.

The treatment of cancer patients with currently available, i.e. largely non-selective, chemotherapeutic agents results often also in undesirable side effects such as weight loss, loss of hair, nausea, and vomiting. The vomiting may be so severe as to be dose-limiting and may even cause life-threatening electrolyte imbalance and nutritional impairment. In order to improve the effect of chemotherapeutic agents and to diminish the side effects it would be extremely important to identify agents that are capable of targeting (homing) to specific organs or tissues or to tumor tissues and to carry the desired cytotoxic or other drugs specifically to these organs or tissues.

Likewise, radiotherapy (whether based on the administration of radioactive substances to the patient or on the use of external radiation sources) is essentially non-selective or has quite limited selectivity. Therefore, improvements such as the availability of agents capable of carrying the radioactive atoms selectively or specifically to the tumor cells or their near vicinity, would be a great advantage.

The same applies also to a specific field of cancer treatment, namely neutron capture therapy, in which a non-radioactive nucleus (e.g. ^{10}B, ^{157}Gd or ^{6}Li) is converted into a radioactive nucleus *in vivo* in the patient with the aid of thermal (slow) neutrons from an external source. In this case, some prior art agents are claimed to have some 2-3 fold selectivity for at least some types of tumors, but the results obtained have been mainly disappointing and negative. Specific targeting agents would offer remarkable advantages also in this field.

Also in the diagnosis of cancer and of metastases (including the follow-up of patients and the study of the effects of treatment on tumors and metastases) more reliable, more sensitive and more selective methods and agents would be a great advantage. This is true for all methods currently in use, such as nuclear magnetic resonance imaging (NMR, MRI), X-ray methods, histological staining methods (for light microscopy and electron microscopy and

related methods, and in the future possibly also NMR, infrared, electron spin resonance and related methods) and in general any imaging as well as laboratory methods (histology, cytology, cell sorting, hematological studies, FACS and so on) known by specialists in the field. Here, agents capable of targeting an entity for detection (a spin label, a radioactive substance, a paramagnetic contrast agent for NMR or a contrast agent for X-ray imaging or tomography, a boron atom for neutron capture and so on) specifically or selectively to tumor tissues, metastases or tumor cells and/or to tumor endothelium would be a great advantage.

Tumors cannot grow and develop beyond ca. 1 mm in diameter if not efficiently supplied with oxygen and nutrients from the blood stream. Consequently, early stage solid tumors may start secreting angiogenic growth factors, such as vascular growth factors (VGFs), vascular endothelial growth factors (VEGFs), angiopoetins and ephrines, into the surrounding tissue. Activated by these factors, new blood vessels sprout from the existing normal blood vessels of the body and enter the tumor, which now is able to grow into life threatening size and malignancy (Folkman, 1997; Kerbel, 2000). This process is called tumor angiogenesis.

Solid tumor growth is angiogenesis-dependent, and a tumor must continuously stimulate the growth of new microcapillaries for continued growth. Tumor blood vessels are structurally and functionally different from their normal resting counterparts. In particular, endothelial cells lining new blood vessels are abnormal in shape, they grow on top of each other and project into the lumen of the vessels. This neovascular heterogeneity depends on the tumor type and on the host organ in which the tumor is growing. Therefore vascular permeability and angiogenesisis are unique in every different organ and in tumor tissue derived from the organ (Folkman, 1999; Brown and Giaccia, 1998).

There are also several nontumor angiogenic conditions other than solid tumors, in which angiogenesis is an important component, e.g. hemangiomas, diabetic retinopathy, arteriovenous malformations, skin circulation disorders, macular degeneration, wound healing and various surgical conditions.

Some conventional therapies have indirect anti-angiogenic effects. E.g. withdrawal of hormone from hormone dependent tumors can downregulate VEGF in tumor cells. The decrease in VEGF causes apoptosis of tumor endothelial cells, whereas the hormone depletion causes apoptosis of hormone-dependent neoplastic cells. During tumor regression, the tumor vessels begin to exhibit a more normal phenotype. However, in these therapies a second wave of angiogenesis occurs and the new blood vessels exhibit similar abnormalities as those of the untreated tumor (Jain, 2001).

When tumors switch to the angiogenic phenotype and recruit new blood vessels, endothelial cells in these vessels express proteins on the luminal surface that are not produced by normal quiescent vascular endothelium (Folkman, 1997). One such protein is $\alpha v\beta 3$ integrin.

Pasqualini et. al. (1997) have identified a peptide that can bind specifically to αvβ3 integrin. This peptide is a nine-residue cyclic peptide containing an ArgGlyAsp (RGD) sequence (US Pat. No. 6,177,542) When injected intravenously the peptide was able to home to blood vessels of murine and human tumors in mice 40–80 fold more efficiently than to those of control organs. It was suggested that RGD peptides may be suitable tools in tumor targeting for diagnostic and therapeutic purposes.

Neri et al. (1997) have reported that single-chain antibody fragments that recognize a splice variant of fibronectin can be used to develop reagents that target tumor vessels.

The tumor vessel specific targets described by Pasqualini et al. (1997) and Neri et al. (1997) are adhesion molecules that mediate binding of endothelial cells to the vascular basement membrane. αvβ3 integrin is found on the endothelial cell surface, where it mediates binding to vitronectin, a component of the vascular basement membrane, where it may act as a ligand for endothelial cell adhesion.

Nicklin et al. (2000) used a peptide, SIGYPLP, for gene transfer into human endothelial cells *in vitro*. Using this peptide as part of an adenovirus surface protein, resting endothelial cells were transfected while vascular smooth muscle cells were not.

It has been shown that peptides binding to and inhibiting the matrix metalloproteinases (MMPs) MMP-2 and MMP-9 *in vitro* are able to suppress tumors in mice. These MMPs are thought to be active for example during proliferation and migration of endothelial cells in angiogenic blood vessels. Proteolytic activity of MMPs is also considered an important aspect of the invasive angiogenic process. MMPs form a protein family that comprises at least 20 distinct enzymes, of which MMP-2 (gelatinase A) and MMP-9 (gelatinase B) are closely associated with angiogenesis. Koivunen et al. (1999) and WO 99/47550 describe cyclic peptides, containing an HWGF motif that are specific inhibitors of MMP-2 and MMP-9. They have also found that the cyclic decapeptide CTTHWGFTLC specifically inhibits the activities of these enzymes, suppresses migration of both tumor cells and endothelial cells *in vitro*, homes to tumor vasculature *in vivo*, and prevents the growth and invasion of tumors in mice.

Hong and Clayman (2000) have described a peptide, TSPLNIHNGQKL, that targets squamous cell cancer cell lines, and becomes internalized into cells *in vitro*. This peptide also targets experimental squamous carcinomas in nude mice. Curnis et al. (2000) have described a bi-functional polypeptide consisting of a targeting motif, NGR, and tumor necrosis factor α (TNFα). This therapeutic agent reduced the tumor burden of mice carrying experimental lymphomas and melanomas. Although the NGR peptide binds to aminopeptidase N, the *in vivo* target of the agent remained unclear since the tumors or their endothelium did not express aminopeptidase N. This peptide also binds fibronectin- and

vitronectin-binding integrins and interferes with cell attachment (US Patent Application No. 6,177,542).

Another therapeutic approach was used by Ellerby et al. (1999; WO 0042973) in experiments with combinatorial peptides. Oligopeptides containing a cyclic targeting and cell internalizing motif, CNGRC or ACDCRGDCFC, and an amino acid sequence that disrupts mitochondrial membranes when inside cells were described. These oligopeptides showed endothelial cell-specific targeting *in vitro* and anti-cancer activity in tumor bearing mice.

US Patent Application No. 5,628,979 describes oligopeptides for *in vivo* tumor imaging and therapy. The oligopeptides contain 4 to 50 peptide units (amino acids), which contain as a characteristic triplet the amino acid sequence Leu-Asp-Val (LDV). This triplet is reported to provide the oligopeptide with *in vivo* binding affinity for LDV binding sites on tumors and other tissues.

Although the prior art describes tumor cell or tumor vasculature homing agents, there is still an enormous need for new agents that would target more specifically tumor tissue or tumor vasculature or both.

Some of the prior art peptides act as inhibitors of e.g. MMPs and show background binding to non-tumor tissues. The fact that MMPs are expressed also in normal tissue throughout the body makes the administration of such peptides (MMP inhibitors) to humans or animals hazardous and even fatal, since the activity of these enzymes is required for normal tissue functions (Hidalgo and Eckhardt, 2001).

For therapeutic applications, targeting peptides have been conjugated to doxorubicin in an uncontrolled fashion, obviously resulting in mixtures of products or at least in an undefined structure and possibly also resulting in unefficient action and especially in difficulties in the identification, purification, quality control and quantitative analysis of the agent, even the amount of doxorubicin per peptide molecule remaining unknown (e.g. Arap et al., 1998). The unspecific conjugation process might also impair the targeting functions of the peptide.

Another very serious disadvantage of the prior art is that most of the described targeting peptides appear to target to the tumor endothelium only and not to the tumor mass itself. For example, the targeting peptide used by Nicklin et al. (2000) directed adenovirus DNA transfection to resting endothelial cells *in vitro*, under conditions that hardly could be applied *in vivo*.

The products, their use and methods according to the present invention offer a highly significant advantage over the prior art in that the products of the invention target to both the tumor endothelium and the tumor cell mass. This fact provides the possibility to target and

destroy both the tumor endothelium supporting tumor growth and the tumor mass itself. A major advantage of this approach comes from the fact that the endothelium is a genetically stable tissue that will not acquire drug resistance but will be irreversibly eliminated.

Also, it is not known whether any of the prior art targeting peptides are universal in the sense of being capable to target to any malignant tumor type. Thus, their use for targeting therapeutic agents to a certain specified tumor may be completely useless, giving no therapeutic advantage or effect over the free therapeutic agent itself. An even more serious drawback is that the use of such targeting agents in diagnostic procedures may not reveal existing tumors and the malignant process may remain unrecognized.

The present invention offers a significant improvement in this respect, since the-targeting agent(s) and unit(s) now described were found to target to all of the various tumor types tested. Remarkably, they target, for example, to Kaposi's sarcoma and ornithine decarboxylase (ODC) overexpressing, highly angiogenic tumors and to human primary melanoma and melanoma metastases *in vivo*.

Further, integrin- and other cell adhesion molecule-targeting agents might be hazardous when administered to patients because they might disrupt the blood vessel walls, while the products of the present invention do not have that drawback.

Finally, if a patient is or becomes allergic to one or more of the prior art targeting peptides and/or other products, the products of the present invention, having a totally different structure, are of course of immense value.

Summary of the Invention

It is an object of the present invention to eliminate the problems of the prior art and to provide novel tumor- and angiogenic tissue targeting agents that comprise one or more targeting unit(s) and one or more effector unit(s). In particular, the invention aims at providing targeting unit(s) comprising one or more motif(s) that are preferably capable of targeting to both tumor endothelium and to tumor cell mass and that therefore as such or linked/ bound/ conjugated/coupled to one or more effector unit(s) are therapeutically and/or diagnostically useful especially for the treatment and diagnosis of cancer, including metastases, and/or useful for cell removal and/or selection and/or sorting and/or enrichment and/or for research.

It is a second object of this invention to provide pharmaceutical and diagnostic compositions comprising one or more targeting agent(s) and/or targeting unit(s) comprising one or more motif(s) capable of specifically targeting to tumors, tumor cells and/or tumor endothelium.

Further, it is a third object of the invention to provide novel diagnostic and therapeutic methods for the treatment and/or diagnosis of cancer.

These and other objects, together with the advantages thereof over known targeting or binding peptides and agents and their use are achieved by the present invention as hereinafter described and claimed.

The present invention is based on the finding that a group of peptides having specific amino acid sequences or motifs are capable of specifically targeting (homing) to tumors *in vivo* and also to tumor cells *in vitro*. In other words, the peptides of this invention when administered to a human or an animal body, are capable of selectively binding to tumors and not to normal tissue in the body of the object.

In addition to the peptides of this invention, also their peptidyl and/or peptidomimetic analogues can be used in this invention. These peptides and their peptidyl analogues and their peptidomimetic analogues that are structurally and/or functionally equivalent to the peptides can thus also be used as targeting units and/or as part(s) thereof.

The targeting unit(s) of this invention may be used as such or linked/bound/conjugated/coupled to one or more effector unit(s). These substances can destroy the tumor(s) or hinder its/their growth. Because the targeting units are also capable of targeting to tumor endothelium, they can be used to destroy the vasculature of tumor cells and to hinder the access of nutrients and oxygen to tumor cells, resulting in starvation of the tumor(s). The targeting units and targeting agents of this invention can target also metastases and therefore they can be used to destroy and/or hinder the growth of metastases. Because early diagnosis of metastases is very important for successful treatment of cancer, an important use of the targeting units and targeting agents of this invention is the early diagnosis of tumor metastases.

In particular, the invention provides novel targeting agents that comprise one or more targeting unit(s) and one or more effector unit(s), according to the description below. Each targeting unit comprises one or more motif(s) capable of specifically targeting and selectively binding to tumors *in vivo*; and preferably to the endothelium, to the stroma and/or to the parenchyma of tumors, or to all three compartments of tumors. The effector unit(s) may comprise one or more therapeutic and/or diagnostic entity/entities, and/or one or more entity/entities that are converted and/or can be converted into such unit(s) and/or one or more other entities as described in detail below.

More specifically, the targeting agents according to the present invention are mainly characterised by what is stated in the characterising part of claim 1.

The targeting units, targeting motifs, peptides and peptidyl analogues and peptidomimetic analogues and compounds according to the present invention are mainly characterised by what is stated in claims 50, 88, 113 and 123, respectively or in other indendent claims directed to these objects.

Salt(s) and/or derivative(s) and/or analogue(s) of one or more of the targeting agents/units/motifs according to the present invention are mainly characterised by what is stated in claims 122 and 147.

The diagnostic compositions and/or pharmaceutical compositions according to the present invention are mainly characterised by what is stated in claims 148 to 152.

Kits for treating and/or diagnosing or for cell sorting or removal or for research purposes according to the present invention are mainly characterised by what is stated in claims 153 to 155.

The therapeutic and/or diagnostic methods according to the present invention are mainly characterised by what is stated in claim 156 and 157

The uses of the present targeting agents/units/motifs/compounds peptides and peptidyl analogues and peptidomimetic analogues and/or salt(s) and/or derivative(s) and/or analogue(s) of one or more of them are mainly characterised by what is stated in claims 157 to 178.

The present invention is also directed to the targeting agents/units/motifs/compounds/ peptides and peptidyl analogues and peptidomimetic analogues and/or salt(s) and/or derivative(s) and/or analogue(s) of one or more of them for use in cancer treatment and/or diagnosis (in the broadest sense of the term cancer).

The present invention is also directed to the use of the targeting agents/units/motifs/compounds/peptides/peptidyl analogues/peptidomimetic analogues and/or salt(s) and/or derivative(s) and/or analogue(s) of one or more of them for the manufacture of a pharmaceutical and/or diagnostic composition for treating and/or diagnosing cancer (in the broadest sense of the term cancer).

Considerable advantages are obtained with the aid of the present invention.

The targeting units and targeting agents of this invention can be used also in conditions other than cancer, such as hemangiomas, diabetic retinopathy, arteriovenous malformations, skin circulation disorders, macular degeneration, wound healing and various surgical conditions. This advantage of the present invention stems from the fact that in all the above conditions, active angiogenesis occurs. Thus, the actively growing endothelial cells express on their surface different molecules than does resting, normal endothelium. The surface

protein expression pattern is similar to that of tumor endothelium, making the use of the targeting units and targeting agents of this invention valuable also in these conditions.

Below, the invention will be described in more detail with the aid of a detailed description and by making reference to the attached drawings.

Detailed description of the invention

For the purpose of this invention, the term "cancer" is to be interpreted in its broadest sense, and includes any disease(s) and/or state(s)/condition(s)/process(es) involving one or more type(s) of transformed and/or malignant cells, including those case(s) where there is no "tumor" (in its narrowest meaning) and/or where the tumor's limit(s)/shape/"border(s)" are difficult and/or impossible to detect and/or define and/or when malignant and/or transformed cells and/or "cancer cells" and/or their like are present/found and/or exist largely and/or only and/or in part as diffuse infiltrate(s) and/or sporadically between/among other cells and/or the matrix and/or their like and/or healthy tissue(s)/organ(s), and/or are present/found and/or exist largely and/or only and/or in part as single cells and/or small group(s) of cells and/or in the blood, lymph, ascites fluid, pleural fluid and/or other fluid(s) and/or exudate(s) and/or their like and/or in the lymph nodes, and so on, and also includes any hematologic(al) malignancy/malignancies/disease(s) and their like, including any leukemias, erythroleukemias diseases such as Waldenström's disease (Waldenström's purpura) and related types of diseases, and their like, and also includes any diseases/conditions/states whose classification as "cancer" is unclarified/unclear/uncertain and/or subject to scientific debate and/or that are "in part" and/or sporadically and/or by some investigators(s)/learned opinion(s) etc. classified as "cancer" and/or "malignancy"/"malignancies", and any other related diseases and states and conditions and their like, in the broadest sense.

The term(s) "amino acid(s)" is/are to be considered and interpreted everywhere herein to comprise and include also any diamino, triamino, oligoamino and polyamino acid(s), as well as also to comprise and include also any dicarboxyl, tricarboxyl, oligocarboxyl and polycarboxyl amino acid(s), as well as any analogous compound(s) comprising more than one carboxyl group and/or more than one amino group.

By the term "peptide" is meant, according to established terminology, a chain of amino acids (peptide units) linked together by peptide bonds to form an amino acid chain. Peptides may also be cyclic as described below. For the purposes of the present invention, also compounds comprising one or more D-amino acids, β-amino acids and/or other unnatural amino acids (e.g. amino acids with unnatural side chains) are included in the term "peptide".

For the purposes of the present invention, the term "peptidyl analogue" means a substance consisting of amino acids (a peptide) that is modified in one or more part(s) thereof in one or

more way(s) so that one or more amino acid(s) is/are converted into or replaced by a modified structural unit (modified amino acid), (e.g. by the introduction or presence of a substituent in a ring or chain, or by the introduction or presence of an "extra" functional group such as an amino, hydrazino, carboxyl, formyl (aldehyde) or keto group, or another moiety, or the absence or removal of a functional group or other moiety), or the structure comprises modifications pertaining to more than one amino acid. The term also includes analogues modified in the amino- and/or carboxy termini, such as peptide amides and *N*-substituted amides, peptide hydrazides, *N*-substituted hydrazides, peptide esters, and their like, and peptides that do not comprise the amino-terminal $-NH_2$ group or that comprise e.g. a modified amino-terminal amino group or an imino or a hydrazino group instead of the amino-terminal amino group, and peptides that do not comprise the carboxy-terminal carboxyl group or comprise a modified group instead of it, and so on. Other similar and related modifications are likewise included. Some examples of possible reaction types that can be used to modify peptides, forming "peptidyl analogues", are e.g. cycloaddition, condensation and nucleophilic addition reactions as well as esterification, amide formation, formation of substituted amides, *N*-alkylation, formation of hydrazides, salt formation etc. Salt formation may be the formation of any type(s) of salt(s), such as alkali or other metal salt(s), ammonium salt(s), salt(s) with organic base(s), acid addition salt(s) etc. Peptidyl analogues may be synthesized either from the corresponding peptides or directly (via other routes).

Compounds can be constructed that structurally and functionally resemble the peptides of the invention, and that do not consist of amino acids or not of amino acids alone, or some or all of whose building blocks are modified amino acids. Different types of building blocks can be used for this purpose, as is well appreciated by those skilled in the art. The function of these compounds in biological systems is essentially similar to the function of the peptides. The resemblance between these compounds and the original peptides is thus based on structural and functional similarities. These compounds are herein called "peptidomimetic analogues", because they mimic the function, conformation and/or structure of the original peptides and, for the purposes of the present invention, their binding activity with respect to the binding to tumors, tumor tissue, tumor cells or tumor endothelium is essentially similar to that of the peptides they resemble. For example, non-peptidyl compounds like benzolactam or piperazine based analogues based on the primary sequence of the original peptides can be used (Adams et al., 1999; Nakanishi and Kahn, 1996a, 1996b; Houghten et al., 1999; Nargund et al., 1998). A large variety of types of peptidomimetic substances have been reported in the scientific and patent literature and are well known to those skilled in the art. Peptidomimetic substances (analogues) may comprise for example one or more of the following structural components: reduced amides, hydroxyethylene and/or hydroxyethylamine isosteres, *N*-methyl amino acids, urea derivatives, thiourea derivatives, cyclic urea and/or thiourea derivatives, poly(ester imide)s, polyesters, esters, guanidine derivatives, cyclic guanidines, imidazoyl compounds, imidazolinyl compounds, imidazolidinyl compounds, lactams, lactones, aromatic rings,

bicyclic systems, hydantoins and/or thiohydantoins as well as various other structures. Many types of compounds for the synthesis of peptidomimetic substances are available from a number of commercial sources (e.g. Peptide and Peptidomimetic Synthesis, Reagents for Drug Discovery, Fluka ChemieGmbH, Buchs, Switzerland, 2000 and Novabiochem 2000 Catalog, Calbiochem-Novabiochem AG, Läufelfingen, Switzerland, 2000). The resemblance between the peptidomimetic compounds and the original peptides is based on structural and/or functional similarities. Thus, the peptidomimetic compounds mimic the properties of the original peptides and, for the purpose of the present application, their binding activity is similar to the peptide(s) that they resemble. Peptidomimetic compounds can be made up, for example, of unnatural amino acids (such as D-amino acids or amino acids comprising unnatural side chains, or of β-amino acids etc.) which do not appear in the original peptides, or they can be considered to consist of or can be made from other compounds or structural units. Examples of synthetic peptidomimetic compounds comprise N-alkylamino cyclic urea, thiourea, polyesters, poly(ester imide)s, bicyclic guanidines, hydantoins, thiohydantoins, and imidazol-pyridino-inoles (Houghten et al. 1999 and Nargund et al., 1998). The peptidomimetic compounds can be characterized as being "structurally and functionally equivalent" to the targeting peptides of this invention.

For the purposes of the present invention the term "peptidomimetic analogue" includes also peptidomimetic substances that are modified in such a way as are peptidyl analogues (as compared to peptides) and/or in related ways.

For the purposes of the present invention, the terms "peptide", "peptidyl analogue" and "peptidomimetic analogue" include also any types of salts, esters, amides, hydrazones, hydroxamic acids and related derivatives/analogues.

For the purpose of the present invention, the term "targeting unit" stands for a compound or a part of a compound, said compound or part of compound being capable of specifically targeting and specifically binding to tumors *in vivo*, and preferably also to tumor stroma, tumor parenchyma, extracellular matrix of tumors and/or tumor endothelium *in vivo*. Another term or synonyme for this specific association is "homing". Targeting and homing mean that the targeting units specifically bind to tumors when delivered/administered to a human or animal body. Delivery/administration may be done systemically, e.g. to the blood circulation. Even non-systemic delivery (e.g. delivery to a limb or organ, or intracranial delivery etc.) may be enough in some cases if systemic delivery is unfavoured or unnecessary. More specifically, the targeting units may, for example, bind to a cell surface, to a specific molecule and/or structure on a cell surface and/or within the cells and/or they may associate with the extracellular matrix present between the cells. The targeting units may also bind to the endothelial cells or the extracellular matrix of tumor vasculature. The targeting units may bind also to the tumor mass or tumor cells or vascular endothelium or extracellular matrix of metastases.

According to this invention, the targeting units bind preferably to tumors *in vivo*. Preferably, the targeting units bind also to tumor endothelium *in vivo*. More preferably, the targeting units of this invention also bind to various angiogenic/neoangiogenic tissues.

Generally, the terms "targeting" or "binding" stand for adhesion, attachment, affinity or binding of the targeting units of this invention to tumors, tumor cells and/or tumor tissue to the extent that the binding can be objectively measured and determined e.g. by peptide competition experiments *in vivo* or on tumor biopsies *in vitro* or by immunological stainings, or by other methods known by those skilled in the art, or can be otherwise objectively proven or detected. Further, the bound substances cannot be essentially washed or rinsed away with normal brief washings with physiological saline or other physiologically acceptable salt or buffer solutions at physiological pH.

The binding of the present targeting agents and/or targeting units to tumors is "selective" which is indicated by the fact that they do not bind to the normal cells or organs, or bind to a much lower degree.

For the purposes of this invention, a "cage-type structure" means an organic or inorganic structure consisting of or comprising multiple rings of any size that forms a three-dimensional cage such as the "cages" of bornanes, norbornanes, camphors and related substances or adamantanes and related structures or carboranes such as *o*-carborane and any related structures.

It has now been surprisingly invented that the three-amino-acid motif Ax- Bx–Cx can effect the targeting, wherein Ax can be I or L, and Bx can be R, and Cx can be D or E, and therefore, peptides comprising one or more motif(s) selected from the group of IRE, IRD, LRE and LRD can be used for targeting.

Further, it has now surprisingly been invented that, more generally, peptides, peptidomimetic analogues and peptidyl analogues consisting of, or comprising, one or more motif(s)

Aa-Bb-Cc

exhibit selective targeting to tumors *in vivo* and to tumor cells *in vitro*;

wherein:

Aa is the L- or D- form of isoleucine, leucine, *tert*-leucine or valine, or a structural and/or functional analogue thereof comprising in its side chain a branched, non-branched and/or alicyclic structure with at least two similar and/or different atoms selected from the group of carbon atoms, silicon atoms, halogen atoms bonded to one or more carbon(s), ether-oxygens and thioether-sulphurs;

Bb is the L- or D- form of arginine, homoarginine or canavanine, or a structural and/or functional analogue thereof comprising at least one guanyl and/or amidino group and/or related group that has or can through protonation obtain a delocalized positive charge; and

Cc is the L- or D- form of glutamic acid or aspartic acid, or a structural and/or functional analogue thereof, comprising in its side chain at least one carboxyl group or esterified carboxyl group;

and/or Aa is Aa′ and/or Bb is Bb′and/or Cc is Cc′, wherein

Aa′ is a branched, non-branched and/or cyclic non-aromatic, lipophilic and/or hydrophobic amino acid or amino acid analogue or derivative or a structural and/or functional analogue thereof, or an amino acid or carboxylic acid or amino acid analogue or derivative or carboxylic acid analogue or derivative that has one or more lipophilic carborane-type and/or other lipophilic boron-comprising side chain(s) and/or its/their equivalent(s) and/or another lipophilic cage-type structure;

Bb′ is an amino acid or amino acid analogue or derivative or a structural and/or functional analogue thereof, that comprises one or more guanyl group(s) and/or amidino group(s) and/or its/their analogue(s) and/or derivative(s) and/or structural and/or functional equivalent(s) and/or one or more group(s) that comprise(s) at least two nitrogen atoms each and has/have or can gain a delocalized positive charge;

Cc′ is an amino acid or amino acid analogue or derivative or a structural and/or functional analogue thereof that comprises: one or more side-chain carboxyl group(s) and/or esterified carboxyl group(s) and/or ketoxime and/or aldoxime and/or hydroxamic acid group(s) and/or ketone- and/or aldehyde-carbonyl(s).

Alternatively, the motif Aa- Bb- Cc as a whole is a structural and/or functional analogue of a structure where Aa, Bb and Cc are as defined above.

Further, it has now been surprisingly invented that, more generally, peptides, peptidyl analogues and peptidomimetic analogues consisting of, or comprising, one or more motifs

$$Dd - Ee - Ff$$

wherein
Dd is either Aa or Bb or Cc or Aa′or Bb′or Cc′, and
Ee is either Aa or Bb or Cc or Aa′or Bb′or Cc′, and
Ff is either Aa or Bb or Cc or Aa′or Bb′or Cc′, and

Dd – Ee – Ff comprises Aa /Aa′and Bb/ Bb′ and Cc/Cc′ , i.e. it is one of the following:

Aa/Aa′- Bb/Bb′- Cc/Cc′ or
Aa/Aa′- Cc/Cc′- Bb/Bb′ or
Bb/Bb′- Aa/Aa′- Cc/Cc′ or
Bb/Bb′- Cc/Cc′- Aa/Aa′ or
Cc/Cc′- Aa/Aa′- Bb/Bb′ or
Cc/Cc′- Bb/Bb′- Aa/Aa′ ,

i.e. the motif comprises the structural parts or units Aa/ Aa′, Bb/Bb′ and Cc/Cc′ in any order, wherein Aa/Aa′ means Aa or Aa′ and Bb/Bb′means Bb or Bb′and Cc/Cc′means Cc or Cc′.

Alternatively, the motif Dd-Ee-Ff as a whole is a structural and/or functional analogue of a structure where Dd-Ee-Ff is as defined above.

Further, it has now surprisingly been invented that targeting agents comprising:

1. one or more targeting units each of which comprises one or more motifs Dd-Ee-Ff

and

2. one or more effector units (to be described in more detail below)

exhibit targeting and selective binding to tumors and cancer and tumor cells and cancer cells and malignant cells and transformed cells and tumor tissues and cancer tissues and malignant tissues and transformed tissues and related cells and tissues and tumor endothelium and activated endothelium and angiogenic endothelium and tumor-endothelium cells and activated-endothelium cells and angiogenic endothelium cells, and their like.

Further, it has now surprisingly been invented that both cyclic and linear and branched peptides and peptidomimetic and peptidyl analogues and targeting agents comprising one or more motif(s) Dd-Ee-Ff exhibit targeting and selective binding to tumors and cancer and tumor cells and cancer cells and malignant cells and transformed cells and tumor tissues and cancer tissues and malignant tissues and transformed tissues and related cells and tissues and tumor endothelium and activated endothelium and angiogenic endothelium and tumor-endothelium cells and activated-endothelium cells and angiogenic endothelium cells, and their like.

Further, it has now surprisingly been invented that peptides and peptidomimetic and peptidyl analogues and targeting agents comprising one or more motif(s) Dd-Ee-Ff and also comprising one or more cyclic structure(s) exhibit targeting and selective binding to tumors and cancer and tumor cells and cancer cells and malignant cells and transformed cells and tumor tissues and cancer tissues and malignant tissues and transformed tissues and related cells and tissues and tumor endothelium and activated endothelium and angiogenic endothelium and tumor-endothelium cells and activated-endothelium cells and angiogenic endothelium cells, and their like.

Further, it has now surprisingly been invented that peptides and peptidomimetic and peptidyl analogues and targeting agents comprising one or more motif(s) Dd-Ee-Ff and also comprising one or more cyclic structure(s) that is/are cyclic by virtue of one or more disulphide bridge(s) exhibit targeting and selective binding to tumors and cancer and tumor cells and cancer cells and malignant cells and transformed cells and tumor tissues and cancer tissues and malignant tissues and transformed tissues and related cells and tissues and tumor endothelium and activated endothelium and angiogenic endothelium and tumor-endothelium cells and activated-endothelium cells and angiogenic endothelium cells, and their like.

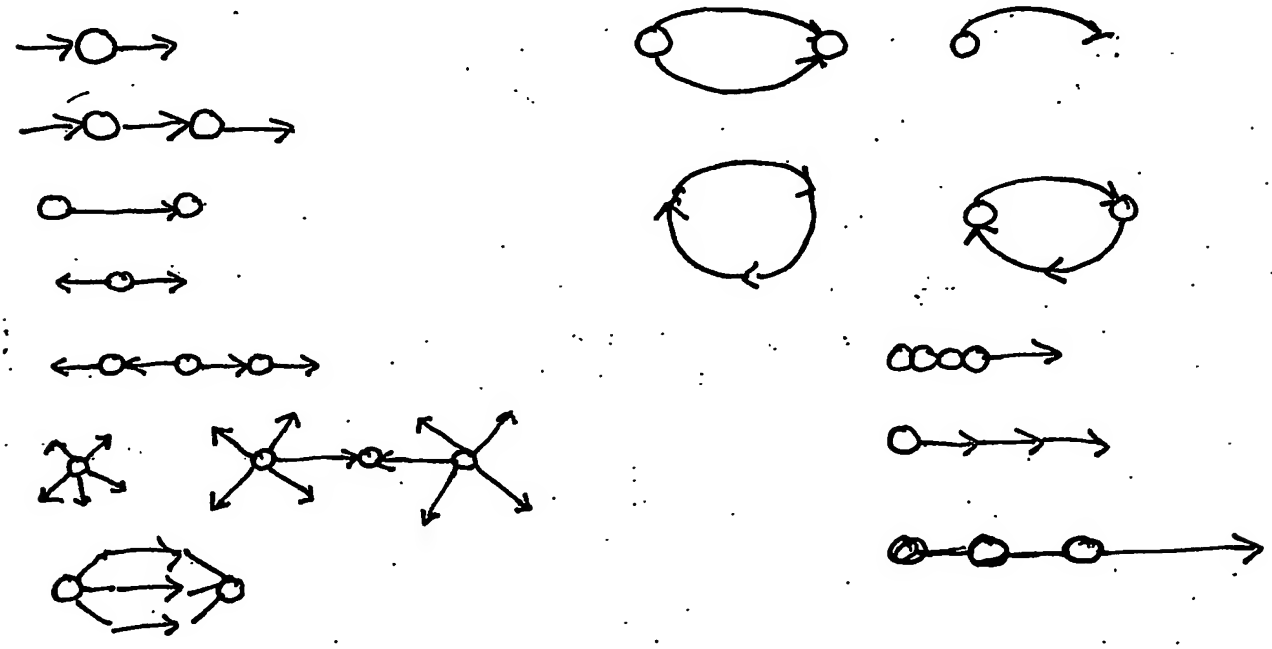
Further, it has now surprisingly been invented that peptides and peptidomimetic and peptidyl analogues and targeting agents comprising one or more motif(s) Dd-Ee-Ff and also comprising one or more cyclic structure(s) that is/are cyclic by virtue of one or more lactam bridge(s) exhibit targeting and selective binding to tumors and cancer and tumor cells and cancer cells and malignant cells and transformed cells and tumor tissues and cancer tissues and malignant tissues and transformed tissues and related cells and tissues and tumor endothelium and activated endothelium and angiogenic endothelium and tumor-endothelium cells and activated-endothelium cells and angiogenic endothelium cells, and their like.

Herein, cyclicity/cyclic and so on refer, if not otherwise noted and/or obvious/evident, to the cyclicity of a peptide, mimete, sequence, motif, targeting agent, targeting unit, targeting motif, and so on, and not merely to the presence of simple ring(s)/cycle(s) etc. in protecting and/or activating group(s), resin constituent(s) and/or side chain(s) of amino acid(s) and/or their analogue(s), etc., as those skilled in the art very well understand.

The inventional motifs, Aa – Bb – Cc as well as Dd – Ee – Ff, as defined above, give rise to the tumor targeting properties of the compounds comprising them, and each motif can be part of a larger structure, such as a peptide (cyclic or non-cyclic) or some other structure, those structures (i.e. structures comprising the motif(s) Aa – Bb – Cc and/or Dd – Ee – Ff)

being included in the invention. Also compounds and structures comprising more than one motif Aa – Bb – Cc and/or more than one motif Dd – Ee – Ff are included in the invention, and in that case the motifs or some of them may be identical and/or similar and/or different, having structures as defined above. When the compound or structure in question consists of or comprises more than one motif Aa – Bb – Cc and/or Dd – Ee – Ff, the orientation and direction of the motifs may vary. All possible modifications and alternatives are included in the invention.

The following schematic representations display some non-limiting possibilities, and in them each arrow indicates a motif Aa – Bb – Cc or Dd – Ee – Ff according to the invention, or a motif whose N-terminal NH_2 group and/or carboxyterminal COOH group have been modified to give NH or N (one or two hydrogens replaced by something else) and –C(=O)- (i.e. OH replaced by something else), or a peptidyl analogue or peptidomimetic analogue thereof, the arrow "starting" from Aa or, respectively, Dd or their corresponding analogues:



Here, all lines and circles represent structures other than the inventional tumor targeting motif(s) Aa – Bb – Cc or Dd - Ee - Ff.

The number of possible structures is thus unlimited. In the targeting agents of the invention, the situation is similar and the targeting agents may comprise any number of Aa-Bb-Cc and/or Dd-Ee-Ff, and any number of identical, similar and/or different effector units, as well as any number of linker units and/or solubility modifier units and/or stabilizer units

and/or charge modifier units and/or spacer units and/or lysis and/or reaction and/or reactivity modifier and/or other related units, as defined below, in any spatial, geometrical or other order or location or in any relation to each other.

According to a preferred embodiment of the invention, in the motif Dd-Ee-Ff, Ee is Bb or Bb′, i.e. preferred motifs of this invention include structures comprising Dd-Bb/Bb′-Ff.

The motifs Aa-Bb-Cc and/or Dd-Ee-Ff exhibit selective binding to tumors *in vivo*. Preferably, they exhibit selective binding to primary tumors, to tumor endothelium and/or tumor metastases *in vivo* and/or to tumor cells *in vitro*. Most preferably the motifs and sequences of this invention bind selectively to any kind of neoangiogenic tissue.

The present invention also includes embodiments/cases wherein two or more motifs overlap, examples of this kind being for example structures comprising sequences such as Aa-Bb-Cc-Bb-Aa.

Aa as defined above can be, for example, one of the following illustrative non-limiting possible structures:

1. an α-amino acid (either an L- or a D-amino acid), whose side chain is one of the following:
   - ethyl
   - propyl
   - 1-methylpropyl (the side chain of isoleucine)
   - 2-methylpropyl (the side chain of leucine)
   - 2,2-dimethylpropyl
   - 1-ethylpropyl
   - *tert*-butyl
   - *tert*-pentyl
   - 3-methylbutyl
   - 2-methylbutyl
   - 1- methylbutyl
   - 1- ethylbutyl
   - 2-ethylbutyl
   - cyclohexyl
   - 2-methylcyclohexyl
   - cyclopentyl
   - 2-methylcyclopentyl
   - 3-methylcyclohexyl
   - cyclobutyl
   - cyclopropyl
   - 2-methylcyclopropyl

- 1- methoxyethyl
- 2- methoxyethyl
- methoxymethyl
- ethoxymethyl
- 2-ethoxyethyl
- 1-ethoxyethyl
- 2-methoxypropyl
- 2,2-dimethoxypropyl
- 1-methylpropyl
- 1-methylbutyl
- 1-methylpentyl
- 1,1-dimethylpropyl
- 1,1-dimethylbutyl
- 1,1-dimethylpentyl
- 1,2-dimethylpropyl
- 1-cyclopropylethyl
- 2-cyclopropylethyl
- cyclopropylmethyl
- 1-cyclopropylethyl
- 1-cyclopropylpropyl
- 2-cyclopropylpropyl
- 3-cyclopropylpropyl
- any cyclobutylalkyl
- 1-ethylpropyl
- 1-methylethyl
- other mono-, di-, tri- or oligoalkyl-alkyl
- other cyclic alkyl or substituted cyclic alkyl or alkyl that is substituted with one or more substituted or unsubstituted cycloalkyl group(s) and optionally one or more alkyl group(s)
- allyl
- vinyl
- 1-methylallyl
- 1-ethylallyl
- 1-ethylvinyl
- 1-propenyl
- 1-methyl-1-propenyl
- 2- methyl-1-propenyl
- 3- methyl-1-propenyl
- 1-ethyl-1-propenyl
- 2- ethyl-1-propenyl
- 3- ethyl-1-propenyl
- 1-methyl-1-butenyl

- 2- methyl-1-butenyl
- 3- methyl-1-butenyl
- 1-ethyl-1-butenyl
- 2- ethyl-1-butenyl
- 1- ethyl-2-butenyl
- 2- ethyl-2-butenyl
- 1- ethyl-3-butenyl
- 2- ethyl-3-butenyl
- 3- ethyl-3-butenyl

2. any optical isomer of any of the following carboxylic acids:
- 4-methylpentanoic acid
- 3- methylpentanoic acid
- 4,4-dimethylpentanoic acid
- 3,4-dimethylpentanoic acid
- 3,3-dimethylpentanoic acid
- 3-methylhexanoic acid
- 4-methylhexanoic acid
- 5-methylhexanoic acid
- 2-ethylpentanoic acid
- 3-ethylpentanoic acid
- 4-ethylpentanoic acid
- 2-cyclopropylpentanoic acid
- 3-cyclopropylpentanoic acid
- 4-cyclopropylpentanoic acid
- 2-methylbutanoic acid
- 3-methylbutanoic acid
- 4-methylbutanoic acid
- 2-cyclopropylbutanoic acid
- 3-cyclopropylbutanoic acid
- 4-cyclopropylbutanoic acid

3. any optical and geometrical isomer of any of the following compounds:

- 2-amino-4-methyl-3-pentenoic acid
- 2-amino-4-methyl-4-pentenoic acid
- 2-amino-5-methyl-3-hexenoic acid
- 2-amino-5-methyl-4-hexenoic acid
- 2-amino-5-methyl-5-hexenoic acid

4. aminosubstituted (*N*-substituted) analogues of the amino-comprising compounds of points 1 and 3 that bear at the amino group

- one methyl, ethyl, propyl, isopropyl or other alkyl group
- one cycloalkyl group
- one 9-fluorenylmethyloxycarbonyl (FMOC) group
- one benzyloxycarbonyl (Cbz) group
- one *tert*-butyloxycarbonyl (BOC) group
- two identical, similar and/or different groups selected from the ones mentioned above in this point (point 4).

Bb as defined above can be for example arginine itself or homoarginine or one of the compounds shown in Table 1 as non-limiting illustrative possibilities.

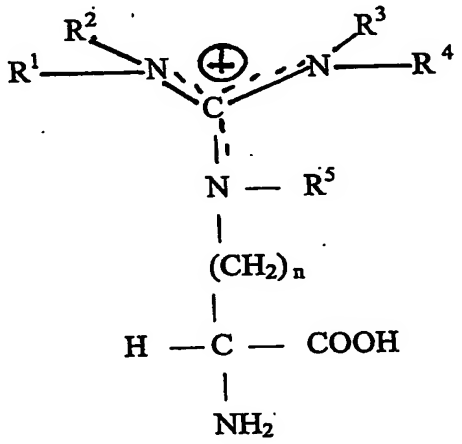


Table 1

R1	R2	R3	R4	R5	n
H	H	H	H	H	1
H	H	H	H	H	2
H	H	H	H	H	5
H	H	H	H	H	6
CH3	CH3	CH3	CH3	CH3	1
CH3	CH3	CH3	CH3	CH3	2
CH3	CH3	CH3	CH3	CH3	3
CH3	CH3	CH3	CH3	CH3	4
CH3	CH3	CH3	CH3	CH3	5
CH3	CH3	CH3	CH3	CH3	6
CH3	CH3	H	H	H	1
CH3	CH3	H	H	H	1
CH3	CH3	H	H	H	2
CH3	CH3	H	H	H	3
CH3	CH3	H	H	H	4
CH3	CH3	H	H	H	5
CH3	CH3	H	H	H	6

CH3	H	CH3	H	H	1
CH3	H	CH3	H	H	2
CH3	H	CH3	H	H	3
CH3	H	CH3	H	H	4
CH3	H	CH3	H	H	5
CH3	H	CH3	H	H	6
CH3	CH3	CH3	CH3	H	1
CH3	CH3	CH3	CH3	H	2
CH3	CH3	CH3	CH3	H	3
CH3	CH3	CH3	CH3	H	4
CH3	CH3	CH3	CH3	H	5
CH3	CH3	CH3	CH3	H	6
H	CH2	- CH2	H	H	1
H	CH2	- CH2	H	H	2
H	CH2	- CH2	H	H	3
H	CH2	- CH2	H	H	4
H	CH2	- CH2	H	H	5
H	CH2	- CH2	H	H	6
H	H	H	H	CH3	1
H	H	H	H	CH3	2
H	H	H	H	CH3	3
H	H	H	H	CH3	4
H	H	H	H	CH3	5
H	H	H	H	CH3	6

wherein CH_2 - CH_2 means that R_2 and R_3 together are - CH_2 - CH_2 -

Cc as defined above can, for example, be one of the following non-limiting illustrative possibilities:

- glutamic acid
- aspartic acid
- any other monoaminodicarboxylic or –tricarboxylic acid
- any other dicarboxylic acid
- any other aminocarboxylic acid comprising an aliphatic or other side chain that comprises one or more carboxyl (COOH) function(s) and/or esterified carboxyl function(s) and/or ketoxime and/or aldoxime and/or hydroxamic acid and/or ketone and/or aldehyde function(s).

Peptides can be synthesized by a large variety of well-known techniques, such as solid-phase methods (FMOC-, BOC-, and other protection schemes, various resin types), solution methods (FMOC, BOC and other variants) and combinations of these. Even

automated apparatuses/devices for the purpose are available commercially, as are also routine synthesis and purification services. All of these approaches are very well known to those skilled in the art. Some methods and materials are described, for example, in the following references:

Bachem AG, SASRIN™ (1999), The BACHEM Practise of SPPS (2000), Bachem 2001 catalogue (2001), Novabiochem 2000 Catalog (2000), Peptide and Peptidomimetic Synthesis (2000) and The Combinatorial Chemistry Catalog & Solid Phase Organic Chemistry (SPOC) Handbook 98/99.

Peptide synthesis is exemplified also in the Examples.

As those skilled in the art well know, it is often advisable, important and/or necessary to use one or more protecting groups, a large variety of which are known by those skilled in the art, such as so-called FMOC, BOC, and trityl groups and other protecting groups mentioned in the Examples herein, and/or to use one or more activators and/or activating agents and so on. Most often, the protecting groups are used for protecting amino, carboxyl, hydroxyl, guanyl and –SH groups, and for any reactive groups/functions.

As those skilled in the art well know, activation often involves carboxyl function activation and/or activation of amino groups.

Protection may also be orthogonal and/or semi/quasi/pseudo- orthogonal. Protecting and activating groups, substances and their uses are exemplified in the Examples and are described in the references including the catalogues mentioned above specifically cited elsewhere herein, and are also described in a large number of books and other sources of information commonly known by those skilled in the art (e.g. Protective Groups in Organic Synthesis, 1999).

Resins for solid-phase synthesis are also well known in the art, and are described for example in the Examples and in the above-cited references (Bachem AG, SASRIN™ (1999), The BACHEM Practise of SPPS (2000), Bachem 2001 catalogue (2001), Novabiochem 2000 Catalog (2000), Peptide and Peptidomimetic Synthesis (2000) and The Combinatorial Chemistry Catalog & Solid Phase Organic Chemistry (SPOC) Handbook 98/99.)

In a preferred embodiment of the invention, the tumor targeting unit(s) or some or at least one of them are/is cyclic and/or form(s) part or parts of a cyclic structure or of cyclic structures and/or part(s) of them or of some or at least one of them are/is cyclic and/or form(s) part or parts of a cyclic structure or of cyclic structures.

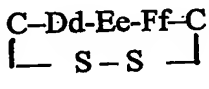
In one especially preferred embodiment of the invention, the tumor targeting unit(s) or some or at least one of them are/is cyclic and/or form(s) part or parts of a cyclic structure or of cyclic structures and/or part(s) of them or of some or at least one of them are/is cyclic and/or form(s) part or parts of a cyclic structure or of cyclic structures in such a way that the motif(s) Aa - Bb - Cc and/or Dd – Ee - Ff or some or at least one of them are/is contained (included) in one or more cyclic structure(s), i.e. all three of the defining moieties (Aa and Bb and Cc; and/or Dd and Ee and Ff) or at least one or some or (preferably) all of the motifs are contained in one or more cyclic structure(s).

In the targeting agents of the invention, the targeting unit(s) or at least some or one of them are/is preferably cyclic or form(s) part or parts of cyclic structures, and/or part(s) of them or of some or at least one of them are/is cyclic and/or form(s) part or parts of a cyclic structure or of cyclic structures, while the effector unit(s) may or may not be included in a cyclic structure or cyclic structures.

Cyclic peptides are usually more stable *in vivo* and in many other biological systems than are their non-cyclic counterparts, as is known by those skilled in the art. The targeting properties also are more pronounced when the targeting unit is cyclic or contained in a cyclic structure, probably because of better orientation of the moieties contained in the targeting motifs and/or because of the more "rigid" structure of the targeting unit.

Of course, the tumor targeting agents, and/or targeting units of the invention may comprise also more than one cyclic structures. This is preferred when there are more than one targeting units.

The cyclic structure may be of any type and may be formed by any method of cyclization or formation of cyclic compounds. Many suitable methods are known per se in the art, and can be used by those skilled in the art. One preferred cyclic structure type is a structure characterized by the presence of a disulphide bond (such as that between the cysteine moieties in many natural substances such as the peptide hormones vasopressin and oxytocin). Non-limiting examples of cyclic structures are, for example, compounds of the formula:

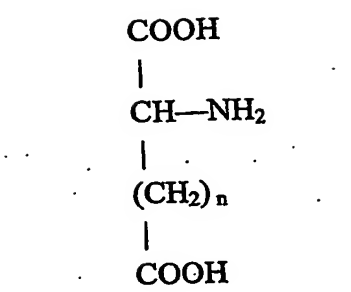


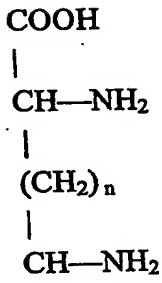
where C-S-S-C indicates a cystine. Because of the easy availability and low price of cysteine, this type of structure is a preferred one. The –S–S– - bridge need not, however, be between cysteine units but may also exist between other amino acids or other moieties comprising –SH groups. Of course, such structures may comprise more than Dd-Ee-Ff between the cysteine units, and may comprise for example one or more amino acid(s) or

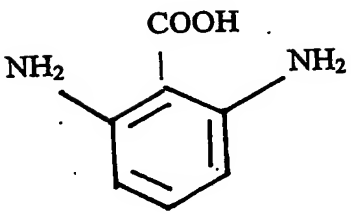
modified amino acid(s) outside the cyclic structure bonded to one or more cysteine units, and so on.

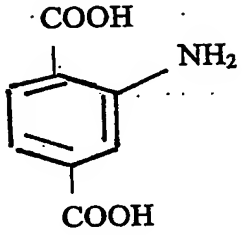
One possibility of forming the cyclic structure(s) is the formation of a peptide bond to give a lactam-type structure. This may be achieved, for example, by methods based on the use of orthogonally protected amino acids. Thus, for example, one amino acid comprising an orthogonally protected "extra" COOH function (e.g the α-allyl ester of *N*-α-FMOC-L-glutamic-acid, i.e., "FMOC-Glu-Oall"), or the α-*tert*-butyl ester of *N*-α-FMOC-L-glutamic acid ("FMOC-Glu-OtBu), or the γ-4{*N*-[1-(4,4-dimethyl-2,6-dioxocyclohexylidene)-3-methylbutyl]-amino}benzyl ester of *N*-α-FMOC-L-glutamic acid ("FMOC-Glu-Odmab") or the γ-2-phenylisopropyl ester of *N*-α-FMOC-L-glutamic acid ("FMOC-Glu(O-2-PhiPr)-OH"), or related derivatives of other dicarboxylic amino acids, such as aspartic acid; or resin-bound forms of any of the aforementioned), and one amino acid with an orthogonally protected "extra" amino group (e.g *N*-α-FMOC-*N*-ε-4-methyltrityl-L-lysine ("FMOC-Lys(Mtt)-OH") or the corresponding derivative of ornithine or some other diaminocarboxylic acid or a resin-bound form of one of these; resin-bound forms, however, not simultaneously with resin-bound forms of the orthogonally protected amino acids with "extra" COOH), may be incorporated in the structure and, after deprotection, the carboxyl and amino groups may be reacted, usually using activator(s). This type of methodology is well known and is described, for example, in the following references Novabiochem Catalog (2000), pp. 19-21 and 33 and specifically B9-B15, and in the references therein, Bachem 2001 catalogue (2001), pp. 31-32, Chan et al. (1995), Yue et al. (1993) and Hirschmann et al. (1998). Suitable starting materials are available commercially, and further ones can be made by methods known in the art. D-amino acid derivatives can also be used in this methodology. Instead of "truly" orthogonal protective groups, also quasiorthogonal/semi-orthogonal/pseudoorthogonal protecting groups can be employed, as those skilled in the art understand.

Cyclic products made by this approach are usually especially stable in biological milieu, and are thus preferred. This type of structures may be produced by any of the methods for the production of such structures (chemical, enzymatic or biological). Many such methods are well known for those skilled in the art. Cyclic structures of this type can be syntesized chemically with the aid of solid-phase synthesis but they can likewise be synthesized using solution methods or a combination of both, as those skilled in the art well know. Amino acids with an "extra" carboxyl or amino function suitable for cyclization purposes (when adequately protected) include (as non-limiting possibilities), for example, those with the structures shown below:









In solution cyclizations of any type, dilute solutions are normally advantageous, as is well known by those skilled in the art.

The synthesis of lactams is exemplified in the Examples, as are also the products of such an approach, and their targeting ability and use.

For example, structures of the following type are included in the invention:

Kk–Dd- Ee- Ff - Ll

wherein Dd, Ee and Ff are as defined herein earlier, and

Kk is any peptide sequence or other structure or a combination of such, and
Ll is any peptide sequence or other structure or a combination of such, or

Kk and Ll are parts of a peptide sequence or other structure or a combination of such (the compound thus being cyclic). Many other possibilities for a cyclic structure or cyclic structures likewise exist that are evident for those skilled in the art.

In a preferred embodiment of the invention, Kk and Ll each comprise a structural fragment (e.g. a functional group) that can be used to form a bond (or linkage) between Kk and Ll so that a cyclic structure is formed, or Kk and Ll are parts of a structure such that the substance Kk – Dd- Ee- Ff- Ll is, in fact, cyclic, i.e. that a link (in addition to Ee) exists that connects Dd and Ff to each other.

Among preferred embodiments of the invention are structures where the motif(s) Aa – Bb – Cc and/or Dd-Ee-Ff or at least one or some of them are selected from the group of Xa – Xb – Xc, wherein

Xa is an α-amino acid (either L- or D- amino acid) of the formula $R^1 - CR^2 (NH_2) - COOH$ and the side chain R^1 is selected from the side chains listed in point 1 on pages ~~18 – 20~~ 17-19, and the side chains R^2 is one of the following: hydrogen, methyl, ethyl, propyl, and

Xb is the L- or D- form of arginine,
homoarginine,
canavanine,
2-amino-8-guanidino-octanoic acid,
2-amino-7-guanidino-octanoic acid,
2-amino-6-guanidino-octanoic acid,
2-amino-5-guanidino-octanoic acid,
2-amino-7-guanidino-heptanoic acid,
2-amino-6-guanidino-heptanoic acid,
2-amino-5-guanidino-heptanoic acid,
2-amino-4-guanidino-heptanoic acid,
2-amino-5-guanidino-hexanoic acid,
2-amino-4-guanidino-hexanoic acid,
2-amino-3-guanidino-hexanoic acid,
2-amino-4-guanidino-pentanoic acid,
2-amino-3-guanidino-pentanoic acid, and

Xc is the L- or D- form of
glutamic acid,
aspartic acid,
2-aminopropanedioic acid,
2-aminohexanedioic acid,
2-aminoheptanedioic acid,
2-aminooctanedioic acid,
or any other 2- aminoalkanedioic acid,

and/or from peptidyl and/or peptidomimetic analogues of one or more these sequences.

Among especially preferred embodiments are structures, where the motif(s) Aa-Bb-Cc and/or Dd-Ee-Ff or at least one or some of them are selected from those given below in Table 2 and/or from peptidyl and/or peptidomimetic analogues of one or more of these specific sequences.

Table 2.

Aa/Dd	Bb/Ee	Cc/Ff
1 L-isoleucine	L-arginine	L-aspartic acid
2 "	"	L-glutamic acid
3 D-isoleucine	D-arginine	D-aspartic acid
4 "	"	D-glutamic acid
5 L-leucine	L-arginine	L-aspartic acid
6 "	"	L-glutamic acid
7 D-leucine	D-arginine	D-aspartic acid
8 "	"	D-glutamic acid
9 L-isoleucine	L-homoarginine	L-aspartic acid
10 "	"	L-glutamic acid
11 D-isoleucine	D-homoarginine	D-aspartic acid
12 "	"	D-glutamic acid
13 L-leucine	L-homoarginine	L-aspartic acid
14 "	"	L-glutamic acid
15 D-leucine	D-homoarginine	D-aspartic acid
16 "	"	D-glutamic acid
17 L-2-aminopentanoic acid	L-arginine	L-aspartic acid
18 D-2-aminopentanoic acid	D-arginine	D-aspartic acid
19 L-2-aminopentanoic acid	L-arginine	L-glutamic acid
20 D-2-aminopentanoic acid	D-arginine	D-glutamic acid
21 L-2-aminohexanoic acid	L-arginine	L-aspartic acid
22 D-2-aminohexanoic acid	D-arginine	D-aspartic acid
23 L-2-aminohexanoic acid	L-arginine	L-glutamic acid
24 D-2-aminohexanoic acid	D-arginine	D-glutamic acid
25 L-2-aminoheptanoic acid	L-arginine	L-aspartic acid
26 D-2-aminoheptanoic acid	D-arginine	D-aspartic acid
27 L-2-aminoheptanoic acid	L-arginine	L-glutamic acid
28 D-2-aminoheptanoic acid	D-arginine	D-glutamic acid
29 L-2-amino-2-ethylbutanoic acid	L-arginine	L-aspartic acid
30 D-2-amino-2-ethylbutanoic acid	D-arginine	D-aspartic acid
31 L-2-amino-2-ethylbutanoic acid	L-arginine	L-glutamic acid
32 D-2-amino-2-ethylbutanoic acid	D-arginine	D-glutamic acid
33 L-isoleucine	L-arginine	2-aminopropanedioic acid
34 D-isoleucine	D-arginine	"
35 L-leucine	D-arginine	"
36 D-leucine	D-arginine	"
37 L-isoleucine	L-arginine	L-2-aminohexanedioic acid
38 D-isoleucine	D-arginine	D-2-aminohexanedioic acid
39 L-leucine	L-arginine	L-2-aminohexanedioic acid
40 D-leucine	D-arginine	D-2-aminohexanedioic acid
41 L-isoleucine	L-arginine	L-2-aminoheptanedioic acid

42	D-isoleucine	D-arginine	D-2-aminoheptanedioic acid
43	L-leucine	L-arginine	L-2-aminoheptanedioic acid
44	D-leucine	D-arginine	D-2-aminoheptanedioic acid
45	L-2-aminopentanoic acid	L-homoarginine	L-aspartic acid
46	D-2-aminopentanoic acid	D-homoarginine	D-aspartic acid
47	L-2-aminopentanoic acid	L-homoarginine	L-glutamic acid
48	D-2-aminopentanoic acid	D-homoarginine	D-glutamic acid
49	L-2-aminohexanoic acid	L-homoarginine	L-aspartic acid
50	D-2-aminohexanoic acid	D-homoarginine	D-aspartic acid
51	L-2-aminohexanoic acid	L-homoarginine	L-glutamic acid
52	D-2-aminohexanoic acid	D-homoarginine	D-glutamic acid
53	L-2-aminoheptanoic acid	L-homoarginine	L-aspartic acid
54	D-2-aminoheptanoic acid	D-homoarginine	D-aspartic acid
55	L-2-aminoheptanoic acid	L-homoarginine	L-glutamic acid
56	D-2-aminoheptanoic acid	D-homoarginine	D-glutamic acid
57	L-2-amino-2-ethylbutanoic acid	L-homoarginine	L-aspartic acid
58	D-2-amino-2-ethylbutanoic acid	D-homoarginine	D-aspartic acid
59	L-2-amino-2-ethylbutanoic acid	L-homoarginine	L-glutamic acid
60	D-2-amino-2-ethylbutanoic acid	D-homoarginine	D-glutamic acid
61	L-isoleucine	L-homoarginine	2-aminopropanedioic acid
62	D-isoleucine	D-homoarginine	"
63	L-leucine	D-homoarginine	"
64	D-leucine	D-homoarginine	"
65	L-isoleucine	L-homoarginine	L-2-aminohexanedioic acid
66	D-isoleucine	D-homoarginine	D-2-aminohexanedioic acid
67	L-leucine	L-homoarginine	L-2-aminohexanedioic acid
68	D-leucine	D-homoarginine	D-2-aminohexanedioic acid
69	L-isoleucine	L-homoarginine	L-2-aminoheptanedioic acid
70	D-isoleucine	D-homoarginine	D-2-aminoheptanedioic acid
71	L-leucine	L-homoarginine	L-2-aminoheptanedioic acid
72	D-leucine	D-homoarginine	D-2-aminoheptanedioic acid

Among the most preferred embodiments of the invention are structures where the motif(s) Aa-Bb-Cc and/or Dd-Ee-Ff or at least some or one of them are selected from the specific sequences given on rows number 1 – 16 (and, especially, on rows 1-8) in Table 2 and/or from peptidyl and/or peptidomimetic analogues of one or more of these specific sequences.

Further, among preferred embodiments of the invention are the structures where one or more of the targeting units have the structure

Gg –Aa-Bb-Cc- Hh or the structure Gg –Dd-Ee-Ff- Hh

wherein the motif(s) Aa- Bb- Cc and/or Dd-Ee-Ff is/are selected from the group of Xa-Xb-Xc as defined above, and/or from peptidyl and/or peptidomimetic analogues of one or more of these sequences, and among especially preferred embodiments are the structures where one or more of the targeting units have the structure Gg-Aa-Bb-Cc-Hh and/or Gg-Dd-Ee-Ff-Hh wherein the motif(s) Aa-Bb-Cc and/or Dd-Ee-Ff are selected from the sequences given in Table 2 and/or from peptidyl and/or peptidomimetic analogues of one or more of those specific sequences, and the structure(s)

Gg – Hh

are/is selected from the following:

a) cystine (i.e., Gg and Hh are cysteines that are connected to each other with a disulphide bridge)
b) two amino acids directly connected to each other via a peptide bond between an amino group of either one of them and a carboxyl group of the other one [either an "extra" amino group (of either Gg or Hh) such as the ε-amino group of lysine or the δ-amino group of ornithine or the *N*-terminal amino group of Gg, and the *C*-terminal carboxyl group of Hh or an "extra" carboxyl group (of either Hh or Gg) such as the ω-carboxyl groups of glutamic and aspartic acids]
c) a cysteine-type structure where Hh and Gg independently of each other are either an amino acid or another structure comprising an "oxidized thiol" moiety and a disulphide bridge existing between them
d) two structures, either one or both of which are/is not an amino acid, connected to each other with a peptide bond in a way analogous to that in point b)
e) a structure consisting of three (3) to twelve (12) amino acids connected to each other with peptide bonds and/or other amide bonds and/or a disulphide bridge or bridges, said structure optionally comprising further targeting units according to the invention.

The formation of disulphide bonds (-S-S-) is well known by those skilled in the art, and a number of prior art methods for this purpose are documented in detail in the literature, as are also many oxidants that can be used for the conversion of two thiol (-SH) groups (e.g. those of two cysteine units) into a disulphide (-S-S-) group. The use of this methodology for the production of cyclic peptides is also very well known. One possibility is simple air oxidation (pure oxygen can of course also be used), and also the use of many other oxidants is straightforward. In some of the examples given below, for example, elementary iodine is being used.

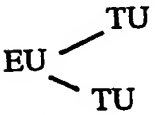
The linking of any units to each other can be performed in solution and/or using solid-phase methods. Specific reaction sequences (to avoid formation of mixtures and/or byproducts) are usually preferred for linking the units of a targeting agent to each other, as is well understood by those skilled in the art. The units may be coupled to each other either using solid-phase synthesis or in solution, or employing both, for each specific case, as is appreciated by those skilled in the art. As those skilled in the art in the art also understand, depending on the exact structure to be synthesized, it may not be necessary (in some cases) to synthesize it from specific parts (units), if the structure can be made otherwise/by other means.

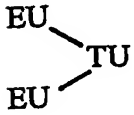
In particular, the tumor targeting units according to this invention comprise (or consist of) one or more identical, similar and/or different motif(s) Aa – Bb – Cc and/or Dd – Ee – Ff, as defined obove. Also compounds consisting of or comprising motifs of different types (i.e., for example, peptide and peptidomimetic motifs, or peptide and peptidyl analogue and peptidomimetic motifs and so on) are included in the invention. Thus, any peptides, any peptidyl and peptidomimetic analogues, and any compounds with structural properties of more than one of these classes of compounds, that comprise at least one motif Aa – Bb – Cc and/or Dd-Ee-Ff as defined above, are included in the invention.

Preferably, the targeting units comprise as few amino acid and/or other units as possible; each one preferably 11 or less, more preferably, 9 or less, still more preferably 7 or less, most preferably 5 or 6.

The ability of the inventional motifs to target to tumors, tumor cells etc. (as described above) or, in general, to target has not been reported or known. The use of these short and easily synthesized motifs for targeting has likewise not been reported or known.

The tumor targeting agents of the invention consist of or comprise one or more identical, similar and/or different motif(s) selected from Aa – Bb – Cc and Dd – Ee – Ff, and one or more identical, similar and/or different effector unit(s), and optionally also one or more identical, similar and/or different unit(s) selected from the following: linker units, solubility modifier unit(s), stabilizer unit(s), charge modifier unit(s), spacer unit(s), lysis and/ or reaction and/or reactivity modifier unit(s), internalizing unit(s) and/or internalization enhancer unit(s) and/or membrane interaction unit(s) and/or other local route and/or local attachment/local binding and/or distribution affecting unit(s),other related units. The units in the tumor targeting agents may be connected/linked/bound/conjugated/coupled to each other by any means suitable for that purpose. Many possibilities are known to those skilled in the art for linking structures, molecules, groups etc. of the types in question or of related types, to each other. The various units may be linked either directly or with the aid of one or more identical, similar and/or different linker units. The tumor targeting agents of the invention may have different structures such as any of the non-limiting types schematically shown below:

1. EU - TU
2. $(EU)_n$ - $(TU)_m$
3. $(EU)_n$ - $(TU)_m$ - $(EU)_k$
4. 

5. 

where EU indicates "effector unit" and TU indicates "targeting unit" and n, m and k are independently any integers except 0. (In these schemes, any optional units have been omitted for simplicity of the presentation).

As always in targeting agents and their like, as well as in many other medicinal and other substances/molecules, it may be wise to include spacer(s) and/or linker(s), such as amino acids and/or their analogues, which may preferably be for example long-chain omega-amino acid(s), to prevent the targeting unit(s) from being 'disturbed' and/or sterically and/or electronically and/or otherwise hindered and/or 'hidden' and so on, by effector unit(s) and/or other unit(s)/part(s) and/or other targeting unit(s), and so on, as those skilled in the art well know. Likewise, it may be wise to include spacer(s) and/or linker(s), such as amino acids and/or their analogues, which may preferably be for example long-chain omega-amino acid(s), to prevent effector unit(s) and/or other unit(s)/part(s) from being 'disturbed' and/or sterically and/or electronically and/or otherwise hindered and/or 'hidden' and so on, by the targeting unit(s) and/or other unit(s)/part(s) and/or other effector unit(s), and so on, as those skilled in the art likewise know.

As in any targeting agents comprising at least one targeting unit and at least one effector unit, it may be of interest and/or value and/or necessary for a good/reliable/strong activity (and so on), to use one or more dendrimeric structure(s) and/or cyclic structure(s) giving an equal opportunity for multiple effector units etc., or any related structure(s) etc., to make it possible to incorporate more than one (and/or several and/or a very large number of and/or an optimum number of) effector units and/or other units per each targeting unit and/or group of targeting units and so on, as is very well known by those skilled in the art. Any such structure(s), embodiment(s) of the invention and so on are also included in the invention, and the Claims are to be interpreted so as to include any such embodiments, structures and/or their like in the broadest sense

Advantages of the targeting units and targeting agents of this invention

There are some serious problems that pertain to any peptides intended for diagnostic and/or therapeutic use(s) or intended for use in the production of targeting agents or other

diagnostic or therapeutic materials. Many of these problems pertain likewise to the production of other types of peptides (and modified peptides) as well. Some of these well-known problems have their origins in the sequence(s) desired, the amino acid residues contained in the sequence(s), and the length of the sequence(s). All of these problems are well known to those skilled in the art.

One problem comes from the length of the sequence: the longer it grows, the more difficult or even impossible the synthesis of the desired product becomes, especially if there are other synthesis problems, such as the presence of difficult residues that require protection-deprotection and/or cause side reactions etc. The tendency to side-reactions and possibly to synthesis termination (that not only decreases the yield of the desired product if this is formed at all, but also gives rise to products with a wrong length of the peptide chain) and formation of serious amounts of harmful by-products, is drastically increased by the presence in the desired sequence of any amino acid(s) that require(s) side-chain protection (e.g., basic side-chains such as those of lysine, histidine and tryptophan) and (of course) also deprotection. All of these problems also make the purification of the desired peptides much more difficult and may make production of adequately purified material impossible.

As compared to many of the prior-art products that comprise long and difficult-to-make sequences with problematic amino acid residues, the peptides of the present invention are clearly beneficial.

Thus, the products and methods and the use of the products of the present invention offer highly significant and very important advantages over the prior art. Such advantages include for example the following ones:

1. The targeting units of this invention can be synthesized easily and reliably. An advantage as compared to many prior art peptides is that the targeting units and motifs of this invention do not need to comprise the problematic basic amino acids lysine and histidine, and also not tryptophan, all of which may cause serious side-reactions in peptide synthesis, and, because of which (if present) the yield of the desired product might be lowered radically. In some cases if the structure comprises one or more such problematic amino acids, it may even be impossible to obtain the desired product in adequate amounts and/or with adequate quality.

In any case, any histidine(s), lysine(s) and tryptophan(s) must be adequately protected using suitable protecting groups that remain intact during the synthesis prodecures. This may be very difficult and at least increases the costs and technical problems. Further, the protective groups used must be such that they can be completely, rapidly and effectively removed at the end of the synthesis and using such reagents, methods and conditions that do not cause side reactions and that do not cause destruction or changes of the product that is being synthetized. Often, deprotection requires more than one treatment because of insufficient deprotection. As those skilled in the art well appreciate, also deprotection may be very

difficult and in some cases cause drastic losses of the product as well as the formation of problematic by-products. Also costs are remarkably increased by the reagents and work load and other costs of the deprotection step or (often) the many steps, and the costs per unit of desired product may be increased still more as the amount of this product may be decreased dramatically because of the side reactions both during the synthesis itself and during the deprotection and also the fact that practically always at least some of the protecting groups are not removed, even a high proportion of the product remaining in a useless protected form that only causes trouble and may even make the whole product useless and dangerous.

2. Because of their smaller size (less amino acid residues) and thus drastically less steps in the synthesis, many of the preferred peptides of the present invention (and the corresponding peptidomimetic and peptidyl analogues) are much more facile and much cheaper to produce than most (if not all) targeting peptides of the prior art. Less reagent types are needed, less reaction steps are needed (coupling steps, deprotection steps, such as removal of FMOC or Boc groups), less side reactions are possible leading to lesser amounts of impurities and lesser types of impurities. The syntheses can be automated and scaled up much more easily and proceed of course much more reliably. Chain terminations occur to a lesser extent than in the case of longer (and, especially, difficult longer) sequences, giving much better economy and also reliability of synthesis.

3. Because histidine is not needed in the products of the present invention, the risk of racemization of it is of course not of concern. As those skilled in the art know, and as stated by Mergler and Durieux (2000): "Trt and Mtt are the most common protecting groups for the protection of the imidazole ring of His. They are stable under the synthesis conditions but are nevertheless not optimal as they do not insure a complete suppression of racemization during the activation".

It is a great advantage not only for the economic synthesis of the products of the present invention but also for the purification and analysis and quality control that any racemization of histidine is outside consideration. It also makes any administration to humans and animals safer and more straightforward.

4. Because of their smaller size, many preferred peptides (and the corresponding peptidomimetic and peptidyl analogues) of the present invention can also be purified much more reliably and easily and with much less labor and apparatus-time, and thus with clearly lower costs. Simpler apparatus may also be enough. (Smaller molecules can usually be purified more easily and more completely and with lower costs as those skilled in the art know.) Costs are thus drastically reduced and better products can be obtained and in greater amounts. Remarkably, the reliability of the purification is much better, giving less concern of toxic remainders and of fatal or otherwise serious side-effects in therapeutic and diagnostic applications, as those skilled in the art very well appreciate.

5. Also because of the fact that their shorter synthesis protocols with relatively few steps produce lesser amounts of lesser types of impurities, many preferred peptides (and likewise the corresponding peptidomimetic substances and peptidyl analogues) of the present invention are highly advantageous. The risks of toxic and even fatal impurities, allergens etc. are dramatically lowered and, in addition, purification is easier.

6. As the difficult basic amino acid residues lysine, histidine and tryptophan are not necessary in the products of the present invention, not only the syntheses are much easier but also the purification of the products is much more straightforward and easy, as is well appreciated by those skilled in the art. This is due to the lack of:

(a) products having one or more protecting groups still present [*i.e.*, the presence of protected residues such as histidine or lysine or tryptophan even after attempts to deprotect the residue(s)]

(b) any residual deprotecting agents (as such specific agents are not needed and thus not used)

(c) any residues of the product(s) formed from the protecting group(s) in the deprotection of lysine, histidine or tryptophan, when those amino acids are not present

(d) any residues of the product(s) formed from the peptide chain itself in the deprotection of lysine, histidine or tryptophan, when those amino acids are not present

(e) products in which the peptide chain has been continued at the epsilon amino group of lysine (or similarly at the 'extra' basic nitrogen in the other basic residues) either alone or in addition to the normal chain continuation at the alpha amino group, in spite of protection of the 'extra' basic functionality or because of the presence of some residues that were devoid of the protecting group or from which it had been inadequately lost

(f) products comprising racemized histidine (as stated above).

7. The analysis and thus the quality control of the products of the present invention is far more easy, and thus far less costly, than that of the longer and/or more 'difficult' peptide sequences with 'difficult' amino acid residues (such as lysine), because of the reasons mentioned in the points above, in analogy with the purification, as those skilled in the art easily understand. Of course, also this reduces the costs. Even more important may be the simultaneous increase in the reliability of the analyses and quality control.

8. As residues such as lysine are not needed in the targeting unit, there is not the risk that the effector (or spacer etc.) units (used to obtain diagnostic and/or therapeutic etc. goals) would

be inadequately connected to those residues (the risk being obvious in the cases where such residues are present). This is a remarkable advantage.

9. Further, the effector (etc.) unit(s) can easily be linked to the peptides and peptidyl analogues and peptidomimetic substances of the present invention using (outside the targeting motif or targeting unit) for example lysine that has been orthogonally protected. There is now namely no risk of simultaneous reaction of any lysine residue in the targeting motif or targeting unit if there are no such moieties in it.

10. Also for cyclization of the peptides of the present invention, lysine (or ornithine) bearing adequate orthogonal (or quasi-, semi or pseudo-orthogonal) protection can easily be used, as the targeting unit can be made without such amino acids. This is an enormous advantage.

11. In the case of the synthesis of targeting agents, the effector unit(s) and possible linker unit(s), spacer unit(s) etc. can be linked to the targeting peptide that is still connected to the resin (in solid phase synthesis) without considering the possibility that the removal of the protecting group(s) of amino acid residues such as lysine will cause destruction of the effector, spacer and/or other unit(s). Similar reasoning applies also to solution syntheses.

As compared to the nine-residue cyclic peptide containing the sequence RGD (US Pat. No. 6,177,542), the preferred peptides of the present invention are far shorter and thus greatly advantageous, as decribed above. As compared to antibody fragments (Neri et al., 1997), the same applies.

As compared to the peptide SIGYPLP (Nicklin et al., 2000), the peptides of the present invention are advantageous in that serine and tyrosine with their side-chain hydroxyls (and the inherent side-reaction risks) are unnecessary, while the peptide of Nicklin et al. (2000) contains both of them.

As compared to the cyclic decapeptide CTTHWGFTLC (Koivunen et al., 1999, and WO 99/47550), many of the peptides of the present invention are shorter, and the peptides of the present invention can be made without the problematic residues histidine and tryptophan, in general, with less amino acids with functional groups in the side chains, thus again being (both synthetically and concerning purification, analysis and quality control) devoid of many of the potential problems of the CTTHWGFTLC peptide.

The peptide reported by Hong and Clayman (2000), TSPLNIHNGQKL, is long and contains the problematic residues histidine and lysine and also serine and threonine. The peptides of the present invention can be made without the potential problems of that sequence, as concerns synthesis and analysis and purification for therapeutic, diagnostic and/or other use.

As compared to peptides as long as 50 amino acid units (US Patent No. 5,628,979), the preferred peptides of the present invention are of course highly advantageous concerning not only synthesis but also purification, analysis and quality control problems.

Thus, in resumé, as compared to many other targeting peptides (or peptides claimed to have targeting properties), the products of the present invention offer significant advantages because of their potentially smaller size (that reduces the production time and costs and gives better yields and also much higher purity of the products) and because there is no need for complicated and difficult-to-synthesize sequences containing even several problematic residues requiring protection (that may be inefficient and in any case usually is far from total) and deprotection(s) that are usually difficult, tedious and labor-intensive and cause severe losses of product, severe formation of by-products (often even as the main or at worst even sole product or products) and drastically complicate purification and may require very tedious and costly and yet unreliable procedures, materials and apparatus as well as highly skilled chemists' intensive labor and may be impossible to scale up to production amounts. The huge costs and, especially, the enormous costs of each unit of the desired product may make such products even obsolete. Another factor that may either make many prior-art products dangerous or even fatal and thus obsolete is the possibility that the products may after any purification attempts contain various by-products (substances in which one or more protective groups or modified protective groups still are present at various positions, the substances formed in the deprotection steps, decomposition products of the substances mentioned, possible polymerized and di- and trimerized etc. substances, deprotection reagents and solvents, shorter sequences than was desired, and so on).

As compared to any targeting motifs and units and agents and related products and materials consisting of or containing/comprising antibodies or antibody fragments or their like, the products and materials described in the present invention, including the inventional targeting agents and targeting units and targeting motifs, are extremely highly advantageous because of several reasons. First of all, the inventional agents and units and motifs can be made quite short (small), which (as described above) is of enormous value concerning avoidance of problems with synthesis, analysis, quality control and so on, and which also leads to enormously better economy and safety and makes any production and use much more facile. The size difference as compared to antibodies and even antibody fragments and their like is extremely remarkable and can be even orders of magnitude. The last mentioned materials may actually even be in practise nearly impossible to synthesize chemically or the costs will at least be massive, as compared to the production costs of highly purified and reliable products of the present invention. In the case of antibodies and their fragments, any products, however they are being made, are also usually less pure and, importantly, are subject to suspicions by those skilled in the art and even by laymen, and may actually never enter the market. Potential immunological and related risks are also obvious in the case of large biomolecules as well as in the case large fragments/analogues etc. thereof: modified large biomolecules/fragments of such may also involve other risks that are extremely

difficult to estimate and predict and, perhaps even more importantly, to exclude. Even allergic reactions must be of great concern with such products, in contrats to small synthetic molecules such as many of the inventional targeting agents and units and motifs etc. of the present invention.

As compared to any targeting motifs and units and agents and related products and materials consisting of or containing/comprising antibodies or antibody fragments or their like, the products and materials described in the present invention, including the inventional targeting agents and targeting units and targeting motifs, are highly advantageous also because their structure can be modified largely, in contrast to that of antibodies and their fragments etc. Thus, only a few amino acids/amino acid analogues and/or related materials are necessary in the case of the preparation of the inventional products of the present invention, and even they can be varied largely if this is needed or desired. One or more kinds of amino acids can be omitted wholly if this is deemed reasonable (e.g., histidine, tryptophan, tyrosine, threonine, lysine etc. are not necessary), and very few functional groups are necessary. On the other hand, in the products of the present invention, it is possible, without disturbing the targeting effect, to include various different structural fragments/parts/units/residues etc. taht can give the product(s) specific properties that are of special value in some cases. For example, aromatic rings, radioiodinated aromatic rings and chelating structures can bve easily be incorporated, as the structure is less strictly determined than that of antibodies and their fragments. (The last mentioned advantage is obvoius even when compared to various other long-chain targeting materials and materials claimed to target.) So, the present invention offers very great advantages over any antibody-type and related products, including antibody fragments and materials comprising such.

Effector units

For the purposes of this invention, the term "effector unit" means a group or molecule or radical or other chemical entity, including atoms, nuclei, many-atom entities, such as molecules and radicals as well as large particles such as colloidal particles and their like, or a liposome or a microgranule or their like or a nanodevice or nanochip or their like, or a combination of any of these, and optionally also one or more chemical structure(s) or their like for the attachment of the constituents of the effector unit to each other and/or other parts of the targeting agent and/or for the stabilization and/or solubility enhancement of the effector unit or part(s) of it and/or for related functions; that:

1. has one or more identical, similar and/or different biological activities, this activity/these activities being different from the sole tumor, tumor mass, tumor cell and/or tumor endothelium targeting function (called herein later "targeting function") of the targeting units of this invention, and/or

2. can be converted, wholly or in part, either from outside of the human or animal patient or

subject or the sample or other material under study or treatment, or invasively e.g. with one or more apparatus(es), radiation(s), treatment(s) and/or material(s) or by the administration of one or more substance(s), or by any means known *per se* or to be invented in the future, into one or more unit(s) that have a biological activity, or more than one identical, similar and/or different biological activities, this activity/these activities being different from the targeting function of the targeting unit(s) according to this invention, and/or

3. is converted in the human or animal body or in a biological sample or other material, by the effect of the properties and/or enzymatic and/or other function(s) and/or conditions, such as pH and/or temperature and/or the aqueous milieu, into one or more units that have a biological activity, or more than one identical, similar and/or different biological activities, this activity/these activities being different from the targeting function of the targeting units of this invention, and/or

4. has one or more identical, similar and/or different activities and/or properties, that can be used directly or indirectly for detection and/or observation and/or qualitative analysis and/or quantitative analysis and/or other quantitation and/or signalling and/or imaging and/or photographing and/or other graphing and/or diagnosing and/or estimation and/or prediction and/or signal amplification and/or their like purpose(s) and/or for one or more procedures used for one or more of these purposes, this activity/this property/these activities/these properties being different from the targeting function of the targeting units according to this invention, and/or

5. can be converted, wholly or in part, either from outside of the human or animal patient or subject or the sample or other material under study or treatment, or invasively e.g. with one or more apparatus(es), radiation(s), treatment(s) and/or material(s) or by administration of one or more substance(s), or by any means known *per se* or to be invented in the future, into one or more unit(s) that have an activity or property, or more than one identical, similar and/or different activities and/or properties, that can directly and/or indirectly be used for detection and/or observation and/or qualitative analysis and/or quantitative analysis and/or other quantitation and/or signalling and/or imaging and/or photographing and/or other graphing and/or diagnosing and/or estimation and/or prediction and/or signal amplification and/or their like purpose(s) and/or for one or more procedure(s) used for one or more of these purposes, this activity/this property/these activities/these properties being different from targeting function of the targeting units according to this invention, and/or

6. is converted in the human or animal body or in a biological sample or other material, by the effect of the properties and/or enzymatic and/or other function(s) and/or conditions such as pH and/or temperature and/or the aqueous milieu, into one or more units that has an activity or property, or more than one identical, similar and/or different activities and/or properties, that can directly and/or indirectly be used for detection and/or observation and/or qualitative analysis and/or quantitative analysis and/or other quantitation and/or signalling

and/or imaging and/or photographing and/or other graphing and/or diagnosing and/or estimation and/or prediction and/or signal amplification and/or their like purpose(s) and/or for one or more procedures used for one or more of these purpose(s), this activity/this property/these activities/these properties being different from the targeting function of the targeting units according to this invention, and/or

7. has the ability to bind to one or more preselected atom(s), molecule(s), part(s) of molecule(s) or ion(s), ion(s), structure(s), compound(s), substance(s), particle(s), liposome(s), virus(es), other micro-organism(s), fragment(s) of cells and/or of micro-organism(s), cells, organelle(s), genetic material(s) and/or their functional and/or structural analogues such as phosphorothioates, and/or the like, and/or any preselected combination(s) of them, including combinations of identical, similar and/or different ones, this ability/these abilities being different from the targeting function of the targeting units according to this invention, and/or

8. can be converted, wholly or in part, either from outside of the human or animal patient or subject or the sample or other material under study or treatment, or invasively e.g. with one or more apparatus(es), radiation(s), treatments and/or materials or by the administration of one or more substances, or by any means known *per se* or to be invented in the future, into one or more unit(s) that have the ability to bind to one or more preselected atom(s), molecule(s), part(s) of molecule(s) or ion(s), ion(s), structure(s), compound(s), substance(s), particle(s), liposome(s), virus(es), other micro-organism(s), fragment(s) of cells and/or of micro-organism(s), cells, organelle(s), genetic material(s) and/or their functional and/or structural analogues such as phosphorothioates, and/or the like, and/or any preselected combination(s) of them, including combinations of identical, similar and/or different ones, this ability/these abilities being different from the targeting function of the targeting units according to this invention, and/or

9. is converted in the human or animal body or in a biological sample or other material, by the effect of the properties and/or enzymatic and/or other function(s) and/or conditions such as pH and/or temperature and/or the aqueous milieu, into one or more unit(s) that have the ability to bind to one or more preselected atom(s), molecule(s), part(s) of molecule(s) or ion(s), ion(s), structure(s), compound(s), substance(s), particle(s), liposome(s), virus(es), other micro-organism(s), fragment(s) of cells and/or of micro-organism(s), cells, organelle(s), genetic material(s) and/or their functional and/or structural analogues such as phosphorothioates, and/or the like, and/or any preselected combination(s) of them, including combinations of identical, similar and/or different ones, this ability/these abilities being different from the targeting function of the targeting units according to this invention, and/or

10. has another desired property and/or activity or more than one such property/properties and/or activity/activities, or can be converted, or is converted in the human or animal body or biological sample or material, into one or more unit(s) with one or more such

property/properties and/or activity/activities.

A biological activity according to point(s) 1-3 in this definition may be, for example, a therapeutic activity, or any other biological activity. Examples of such therapeutic activities are for example, cytotoxic activities, cytostatic activities, ability to cause differentiation of cells or to increase their degree of differentiation or to cause phenotypic changes or metabolic changes, chemotactic activities, immunomodulating activities, pain relieving activities, radioactivity, ability to affect the cell cycle, ability to cause apoptosis, hormonal activities, enzymatic activities, ability to transfect cells, gene transferring activities, ability to mediate "knock-out" of one or more genes, ability to cause gene replacements or "knock-in", antiangiogenic activities, ability to collect heat or other energy from external radiation or electric or magnetic fields, ability to induce, reduce, stop and/or otherwise affect transcription and/or translation and/or replication of the cell's genetic information and/or external related information and/or to affect post-transcriptional and/or post-translational events, and so on.

The methods that can be used as described in points 2, 5 and 8 above may be, for example, the use of thermal (slow) neutrons (to make suitable nuclei radioactive by neutron capture), or the administration of an enzyme capable of hydrolyzing for example an ester bond or other bond(s) or the administration of a targeted enzyme according to the present invention, and so on.

The activities and properties mentioned in points 4-6 in the above definition may be, for example, radioactivity, paramagnetism, ferromagnetism, ferrimagnetism, or any type of magnetism, or ability to be detected by NMR spectroscopy, or ability to be detected by EPR (ESR) spectroscopy, or suitability for PET and/or SPECT imaging, or the presence of an immunogenic structure, or the presence of an antibody or antibody fragment or antibody-type structure, or the presence of a gold particle, or the presence of biotin or avidin or other protein, and/or luminescent and/or fluorescent and/or phosphorescent activity or the ability to enhance detection of tumors, tumor cells, endothelial cells and metastases in electron microscopy, light microscopy (UV and/or visible light), infrared microscopy, atomic force microscopy or tunneling microscopy, and so on.

The ability to bind, as indicated in points 7-9, includes for example any of the following non-limiting examples, or any combination of them:

a) the ability to bind to a substance or structure such as a histidine or other tag and/or a peptide and/or protein comprising such a tag

b) the ability to bind to biotin and/or its analogues and/or derivatives (e.g. by virtue of the well-known biotin-binding substance avidin or a fragment or derivative of it)

c) the ability to bind to avidin (e.g. caused by the presence of one or more biotin fragment(s) or their analogues, as is well appreciated by those skilled in the art)

d) the ability to bind to an enzyme or a modified enzyme

e) the ability to bind a metal ion or several metal ions e.g. by chelation or by any means known *per se* or to be invented in the future

f) the ability to bind a substance able to cause cytotoxic and/or apoptotic and/or metabolic effects, or a substance capable of being converted *in situ* into an apoptotic substance, i.e. a pro-apoptotic substance

g) the ability to bind to integrins and/or their like, and/or to any other substances and/or structures involved in cell adhesion and/or migration and/or inter- and/or intracellular signaling

h) the ability to bind to phages

i) the ability to bind to lymphocytes or other blood cells or subgroups of them

j) the ability to bind to any preselected material(s) by virtue of the presence of one or more antibodies and/or their fragments and/or analogues and/or structures selected by biopanning using any preselected material(s) different from tumors or tumor cells or tumor vasculature, and so on,

k) the ability to bind to one or more material(s) that can be used for signal production and/or amplification,

l) the ability to bind to one or more therapeutic substance(s) or the like, etc.

Such binding may be the result of e.g. chelation, formation of covalent bond(s), antibody-antigen-type affinity, ion pair or ion associate formation, specific interactions of the avidin-biotin-type, and/or the result of any type(s) or mode(s) of binding or affinity.

One or more effector unit(s) and/or part(s) of them may also be a part of the targeting unit(s) themselves. Thus, the effector unit(s) may for example be one or more atoms or nuclei of the targeting unit(s), such as one or more radioactive atoms and/or atoms that can be made radioactive and/or paramagnetic atoms and/or atoms that are easily detected by MRI or NMR spectroscopy (such as carbon-13). Further examples are, for example, boron-comprising structures such as carborane-type lipophilic side chains.

The effector unit(s) may be linked to the targeting unit(s) by any type of bond(s) and/or structure(s) and/or any combinations of them that are strong enough so that most, or preferably all or essentially all of the effector units of the targeting agents, when administered or otherwise used, remain linked to the targeting unit(s) during the essential (necessary) targeting process e.g. in a human patient or subject or animal patient or subject or in a biological sample under study or treatment.

The effector unit(s) or some of them and/or part(s) of them may remain linked to the targeting unit(s) or some of them, or it/they or part(s) of it/them may be in part or completely hydrolyzed or otherwise disintegrated from the latter, either by a spontaneous chemical reaction or equilibrium or by a spontaneous enzymatic process or other biological process, or as a result of an intentional operation or procedure such as the administration of one or more hydrolytic enzyme(s) and/or other chemical substance(s). It is also possible that the enzymatic process or other reaction is caused or enhanced by the administration of a targeted substance such as an enzyme in accordance with the present invention.

One possibility is that the effector unit(s) or part(s) them are hydrolyzed from the targeting agent and/or hydrolyzed into smaller units by the effect of one or more of the various hydrolytic enzymes present in tumors (e.g., intracellularly and/or in the cell membrane and/or in the extracellular matrix) and/or in their near vicinity.

Taking into account that the targeting according to the present invention may be very rapid, even non-specific hydrolysis that occurs everywhere in the body may be acceptable and usable for hydrolysing one or more effector unit(s) intentionally, since such hydrolysis may in suitable cases (e.g., steric hindrance, or even without any such hindering effects) be so slow that the targeting agents are safely targeted in spite of the presence of hydrolytic enzymes of the body, as those skilled in the art very well understand. The formation of insoluble products and/or products rapidly absorbed into cells and/or bound to their surfaces after hydrolysis may also be beneficial for the targeted effector units and/or their fragments etc. to remain in the tumors or their closest vicinity.

In one preferred embodiment of the invention, one or more effector unit(s) comprise(s) one or more structure(s), feature(s), fragment(s), molecule(s) and/or the like that make possible and/or cause directly and/or indirectly, the "amplification" of one or more therapeutic effect(s) and/or of other effect(s) and/or phenomenon/phenomena and/or of signal detection, observation, formulation, quantification and/or the like or of the binding of one or more preselected substance(s), material(s) including biological material(s), molecule(s), ion(s), microbe(s), cell(s), and/or the like, and/or the amplification of any desired effect(s), phenomenon/phenomena and/or the like.

Such "amplification" may, for example, be based on one or more of the following non-limiting types:

- the binding, by one or more effector unit(s), of one or more material(s) that can further bind other substances (for example, antibodies, fluorescent antibodies, other "labelled" substances, substances such as avidin and/or other proteins), preferably so that several molecules and/or other "unit(s)" of the further material(s) will/can be bound per each effector unit (applicable for example in the study of histological samples, but also in *in vivo* diagnostics and *in vivo* therapy as well as *in vitro* therapy, cell sorting and many other applications of the invention);
- the effector unit(s) or one or some of them comprise each more than one part(s), portion(s), fragment(s), structure(s) and/or the like capable of binding e.g. a protein, thus making direct amplification possible;
- amplification in more than one steps.

Amplification is possible even in the case of targeting unit(s).

Amplification is possible also for research applications.

Important effector unit types include, as non-limiting possibilities, for example the following:

- cytostatic agents
- cytotoxic agents
- apoptosis enhancing agents
- agents causing apoptosis
- enzyme inhibitors
- enzymes
- antimetabolites
- agents capable of disturbing membrane function(s)
- agents capable of disturbing ion channel function(s)
- agents capable of acting as artificial ion channel(s)
- radioactive substances
- substances capable of emitting α- radiation
- substances capable of emitting β- radiation
- substances capable of emitting γ- radiation
- substances capable of emitting positrons
- substances comprising one or more paramagnetic atom(s)
- substances comprising one or more metal ion(s)
- substances comprising one or more paramagnetic metal ion(s)
- substances comprising one or more radioactive metal ion(s)
- substances comprising one or more unpaired electron(s)
- substances comprising one or more atom(s) of boron
- substances comprising one or more atom(s) and/or ion(s) of gadolinium
- substances comprising one or more atom(s) and/or ion(s) of litium
- substances comprising one or more atom(s) and/or ion(s) of boron-10

- substances comprising one or more atom(s) and/or ion(s) of gadolinium-157
- substances comprising one or more atom(s) and/or ion(s) of litium-6
- substances suitable for neutron capture therapy
- substances comprising one or more type(s) of enriched isotope(s)
- substances comprising enriched radioactive isotopes
- substances comprising enriched nuclei/atoms suitable for NMR spectroscopy and/or imaging
- substances comprising enriched boron-10
- substances comprising enriched gadolinium-157
- substances comprising enriched litium-6
- substances comprising enriched carbon-13
- substances comprising radioactive iodine
- substances comprising tritium
- substances comprising carbon-14
- labelled substances
- biotin and its analogues and derivatives
- substances comprising biotin and its analogues and derivatives
- avidin
- other proteins
- substances comprising avidin
- asparaginase
- intercalators and substances comprising them
- polyamine antimetabolites
- reactive inorganic substances
- oxidants
- reducing agents
- nucleotides and their analogues
- nucleosides and their analogues
- metal chelates
- chelating agents
- substances comprising one or more platinum atom(s) and/or ion(s)
- substances comprising one or more copper atom(s) and/or ion(s)
- substances comprising one or more copper(II) ion(s)
- substances comprising one or more copper(I) ion(s)
- substances comprising radioactive copper atom(s) and/or ion(s)
- cisplatin and its analogues and derivatives
- other platinum antitumor agents and their analogues and derivatives
- copper chelates
- agents disturbing polyamine metabolites and/or uptake and/or function(s) and/or other processe(s) involving polyamine(s) in one or more way(s)
- polyamine analogues and derivatives
- antitumor alkaloids and their analogues and derivatives and sub-structures thereof

- taxol/paclitaxel and its analogues
- bleomycins and their analogues and derivatives
- copper bleomycines and their analogues and derivatives
- bis(thiosemicarbazones) and their analogues and derivatives
- alkylating agents and related substances
- nitrogen mustards and related substances
- ethylenediamine tetraacetic acid (EDTA) and their analogues
- diethylenetriamine pentaacetic acid (DTPA) and their analogues
- polycarboxylic acids and related substances
- metal complexes of ethylenediamine tetraacetic acid (EDTA) and their analogues
- metal complexes of diethylenetriamine pentaacetic acid (DTPA) and their analogues
- metal complexes of polycarboxylic acids and related substances.

In a highly preferred embodiment of the invention, one or more effector unit(s) are and/or comprise one or more alpha emittors (radioactive atom or nuclei capable of emitting alpha particles).

In further preferred embodiments of the invention, one or more effector units are and/or comprise one or more of the following:

- copper chelate(s) such as *trans*-bis(salicylaldoximaro) copper(II) and its analogues
- platinum compound(s) such cisplatin, carboplatin and/or their analogu(s) and/or derivative(s).

In cell sorting and any related application, the targeting unit(s) and/or agent(s) and/or the peptide(s) of the invention can, for example, be used
a) as coupled/linked and/or connected to magnetic particles,
b) as adsorbed, coupled, linked or connected to plastic, glass and/or other solid, porous, fibrous material-type and/or other surface(s) and the like,
c) as adsorbed, covalently bonded and/or otherwise linked, coupled or connected into and/or onto one or more substance(s) and/or material(s) that can be used in columns and/or related systems
d) as adsorbed, covalently bonded and/or otherwise linked, coupled or connected into and/or onto one or more substance(s) and/or material(s) that can be precipitaed, centrifuged and/or otherwise separated, removed and/or the like

The invention also includes kits for these and/or similar purposes.

The targeting agents and targeting units of the present invention may optionally comprise also one or more unit(s) that are intended for one or more of the purposes indicated below:

1. linker unit(s), i.e. unit(s) whose task is to bind, link, couple, bond or connect to each other either one or more targeting unit(s) and/or one or more effector unit(s) and/or one or more unit(s) indicated below in points 2-9;

2. solubility modifier unit(s), i.e. unit(s) that are intended to enhance, decrease and/or otherwise modify the solubility (e.g., aqueous solubility, solubility in a specific vehicle or solvent, fat solubility, and so on) of the targeting unit(s) and/or targeting agent(s) and/or their hydrolysis product(s) and/or other products and/or part(s) of them;

3. stabilizer unit(s), i.e. unit(s) that stabilize the structure of the targeting units(s) and/or targeting agent(s) and/or their hydrolysis product(s) and/or part(s) of them, or stabilize them against reactions and/or reactive substances and/or hydrolytic and/or other enzymes, e.g. during the synthesis, modification, processing, storage and/or use of the of the targeting units(s) and/or targeting agent(s) and/or part(s) of them and/or the starting materials of any of these, and/or *in vivo* and/or *in vitro* during the administration and/or use of the targeting units(s) and/or targeting agent(s) and/or after the targeting units(s) and/or targeting agent(s) have reached their target, and/or the hydrolysis product(s) and/or other products and/or part(s) of them after their release;

4. charge modifier unit(s), i.e. units that increase, decrease and/or otherwise modify the electrical charge(s) of the targeting units(s), targeting agent(s) and/or their hydrolysis product(s) and/or other products and/or part(s) of them and/or one or more starting material(s) of them;

5. spacer unit(s), i.e. unit(s) intended for increasing the distance between specific units or parts in the targeting units(s) and/or targeting agent(s) and/or their hydrolysis product(s) and/or part(s) of them and/or parts of their starting materials, or to release or decrease steric hindrance and/or structural strain (such as angle strain) or their like, or for similar or related purposes;

6. lysis and/ or reaction and/or reactivity modifier unit(s), i.e. units whose task is to make possible, and/or to enhance, and/or to make more rapid, and/or to prevent, and/or inhibit, and/or to make more slow, and/or to quantitatively and/or qualitatively modify, and/or to change and/or modify the course and/or products of, and/or to alter the prerequisites and/or optimal conditions of, and/or to redirect, one or more hydrolytic and/or other lytic reaction(s) and/or other decomposition process(es) and/or reaction(s) and/or their continuation process(es) and/ reaction(s) of the targeting unit(s) and/or targeting agent(s) and/or one or more starting material(s) and/or constituents thereof and/or one or more of their product(s) of hydrolysis and/or of other type(s) of lysis and/or of decomposition and/or of reaction(s); these units also including unit(s) that increase the susceptibility of the targeting agent(s) and/or targeting unit(s) to one or more type(s) of enzymatic and/or non-

enzymatic reaction(s) and/or process(es), such as for example the hydrolysis of one or more effector unit(s);

7. internalizing unit(s) and/or internalization enhancer unit(s) and/or membrane interaction unit(s) and/or other local route and/or local attachment/local binding and/or distribution affecting unit(s), i.e. units that enhance and/or make more rapid and/or cause and/or give rise to and/or prevent and/or inhibit and/or affect in one or more way(s) one or more process(es) that affect and/or determine and/or cause and/or modify the route and/or fate and/or further localization in the vicinity of the targeted area of the targeting agent(s) and/or targeting unit(s) and/or product(s) of their hydrolysis and/or other lysis and/or decomposition and/or other reaction, and/or any related unit(s), such units including for example units capable of causing the internalization of the targeting agent(s) and/or targeting unit(s) and/or effector unit(s), and/or the binding of one ore more of them onto and/or into cell membranes after the targeting unit(s) and/or targeting agent(s) have reacted their target(s);

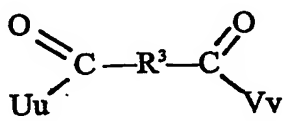
8. adsorption enhancer unit(s), such as fat soluble structures and/or water soluble structures that may or may not be hydrolyzed or otherwise lost, e.g. (after absorption) in the blood or in general in the body;

9. other related unit(s).

Any of the units mentioned in points 1-9 above may be any unit(s) that can be used for such purposes and/or any unit(s) whose ability to perform such function(s) is evident to those skilled in the art. A large number of suitable linker units are known by the prior art. Thus, the linker units may include, for example, one or more of the following non-limiting possibilities:

1. For linking two or more units each comprising an amino group:

- cyclic acid anhydrides (the anhydrides of bivalent or multivalent carboxylic acids)
- dicarboxylic or multivalent carboxylic acids or wholly (all carboxyls) or in part (e.g. one carboxyl per molecule) activated or other (non-activated) derivatives thereof (e.g. anhydrides, acyl chlorides, activated esters, esters with no or a limited degree of activation etc.), e.g. compounds of the type



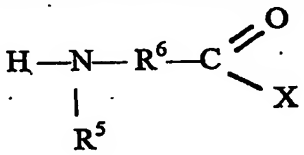
where Uu and Vv may be the same or different [(e.g. each of them may be one of the following: OH, OR^4, Cl, Br, O-C(=O) R^4)] and R^3 and R^4, independent of each other, is for example an alkyl, aryl, aralkyl, cycloalkyl, alkenyl or other hydrocarbon-type group.

- compounds with two or more reactive halogens
- compounds with at least one reactive halogen atom and at least one carboxylic group or its derivative. The amino groups or some of them may be activated before reaction. Specific activators may also be employed for performing the reaction(s), as is understood by those skilled in the art.

2. For linking two or more units each comprising at least one carboxyl group or a derivative of a carboxyl group (such as acyl halide, anhydride and/or ester):

- compounds with at least two similar or different groups selected from the following: amino, substituted amino (-NHR), hydroxyl (alcohol), $-NHNH_2$ or substituted forms thereof, other groups known in the prior art for formation of bonds with carboxyl groups and/or their derivatives. (Activators may be used). Here R^7 is H or any hydrocarbon-type structure or related structure.

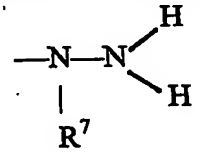
3. For linking an amino group and a carboxyl group:

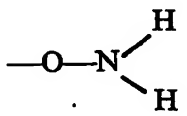


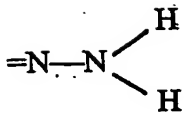
where R^5 is hydrogen or an alkyl, aryl, aralkyl, alkenyl or other hydrocarbon-type radical, and R^6 is for example $(CH_2)_n$ (n = 1 or greater) or an aromatic ring or cycloalkyl group or other hydrocarbon-type structure, or R^5 and R^6 belong to a ring structure, and X is e.g. OH, OR, O-C(=O)R or halogen. Here R^7 is H or any hydrocarbon-type structure or related structur

4. For linking a formyl group or a keto group to another group:

- a compound comprising e.g. at least one of the following groups:







in addition to a group capable of being linked to the unit to which a link is also to be joined. Here R^7 is H or any hydrocarbon-type structure or related structure.

5. For linking several amino-comprising units:
- polyvalent carboxylic acids and/or other polycarboxylic substances such as ethylenediamine-tetraacetic acid (EDTA), diethylenetriaminepentaacetic acid (DTPA) and their like
- anhydrides, esters and acyl halides of polycarboxylic acids and/or of their analogues such as EDTA or DTPA.

6. For linking a substance comprising an amino group to a substance comprising either a formyl group or a carboxyl group: hydrazinocarboxylic acids or their like, such as hydrazinobenzoic acids and aliphatic hydrazinocarboxylic acids, preferably so that the hydrazino moiety is protected e.g. with a 9-fluorenylmethylcarboxyl (FMOC) group and/or the carboxyl group is protected and/or activated. One such compound is 4-(FMOC-hydrazino)benzoic acid that is commercially available. Activators may be needed and used.

7. For linking an organic structure to a metal ion:
- substances that can be coupled to the organic structure (e.g. by virtue of their COOH group(s) (coupling to NH_2) or their NH_2 group(s) (coupling to COOH) or are integral parts of the organic structure, and in addition comprise a polycarboxylic part (a polycarboxyl acid-type structure or for example an EDTA- or DTPA-like structure).
- peptide, peptidyl analogue or peptidomimetic structures comprising several histidine units and/or their like
- peptide, peptidyl analogue or peptidomimetic structures comprising several cysteines and/or other amino acids and/or other structural moieties comprising an –SH group each
- other chelating agents that comprise one or more functional group(s) that can be used to link them to the organic structure in question.

A large variety of prior art substances of the types described above for linking purposes are known to those skilled in the art. Many other types of suitable linking agents are also known in the prior art and are well known by those skilled in the art.

In the case of linking, with any type(s) of linker(s), the linker unit(s) and/or one or more of the unit(s) which are to be connected may have to be and/or may preferable be protected and/or activated, as those skilled in the art well know, and specific activators and/or related substances, temperatures, solvents etc. may be necessary or advantageous, as those skilled in

the art also well appreciate. The same is also true in the case of direct linking of any types of units and structures without using specific linking units.

In order to link (couple) units (compounds) that comprise one or more amino group(s) to units that comprise one or more carboxyl group(s), no linker unit is usually necessary (for the linking purposes alone), if steric hindrance is not present, but for example amino acids or related structures can be used (α, β, γ, etc. and ω-amino acids). ω-amino acids are often preferred because of spacer effects and less crowding/steric hindrance.

A large number of suitable solubility modifier units are known in the prior art, and many others suitable for the purpose are self-evident for those skilled in the art. Suitable solubility modifier units comprise, for example, the following non-limiting possibilities:

for increasing aqeous solubility; the following groups, and/or molecules and/or ions and/or groups comprising one or more identical, similar and/or different ones of them:

- SO_3^-
- $O\text{-}SO_3^-$
- COOH
- COO^-
- NH_2
- NH_3^+
- the guanidino group (protonated or non-protonated)
- the amidino group (protonated or non-protonated)
- other ionic and ionizable groups
- OH
- sugar-type structures;

for increasing fat solubility and/or solubility in organic solvents: any of the following groups, and/or molecules and/or ions and/or radicals comprising one or more identical, similar and/or different ones of them:

- aliphatic (especially long) branched and/or non-branched alkyl and alkenyl groups
- cyclic non-aromatic groups such as the cyclohexyl group
- aromatic rings
- steroidal structures, etc.

A large number of units known or self-evident for those skilled in the art can be used as stabilizer units, e.g. bulky structures (such as *tert*-butyl groups, naphthyl and adamantyl and related radicals etc.) for increasing steric hindrance and D-amino acids and other unnatural amino acids (including β-amino acids, ω-amino acids, amino acids with very large side chains etc.) for preventing or hindering enzymatic hydrolysis etc.

Units comprising positive, negative or both types of charges can be used as charge modifier units, as can also structures that are converted or can be converted into units with positive, negative or both types of charges.

Spacer units may be very important, as is well appreciated by those skilled in the art, and the need to use one or more such units depends on the other components of the structure (e.g. the type of biologically active agent(s) used, and their mechanisms of action) and the synthetic procedures used etc., as is well appreciated by those skilled in the art.

Suitable spacer units may include for example long aliphatic chains (e.g. 3-25 C atoms long) or sugar-type structures (to avoid too high lipophilicity), or large rings, etc. An enormous number of suitable compounds are available in the prior art, and many others are self-evident for those skilled in the art. One group of suitable and often preferred spacer units are ω-amino acids with long chains. The last mentioned compounds can also be used (simultaneously) as linker units between an amino-comprising unit and a carboxyl-comprising unit. Many such compounds are commercially available, both as such and in the forms of various protected derivatives.

Different types of structures, substances and groups are known in the prior art that can be used to cause or enhance e.g. the internalization of peptides and/or other substances into cells, including for example the Antennepedia homeodomain sequence RQIKIWFQNRRMKWKK; Penetratin (Prochiantz, 1996; 1999), as well as stearyl derivatives (Promega Notes Magazine, 2000).

As an apoptosis-inducing structure, for example, the peptide sequence KLAKLAK that interacts with mitochondrial membranes inside cells, can be included (Ellerby et al., 1999).

Units that are susceptible to hydrolysis (either spontaneous chemical hydrolysis or enzymatic hydrolysis by the body's own enzymes and/or targeted and/or non-targeted enzymes administered to the patient) may be very advantageous in cases where it is pertinent that the effector unit(s) or some or one of them are/is liberated from the targeting agent(s) e.g. for internalization and/or for better DNA binding or receptor binding intra- or extracellularly, and so on. Suitable units for this purpose include, for example, structures comprising one or more ester functionalities and/or acetal functionalities and/or other groups and structures known in the prior art. Various protease cleavage site(s) are also well known in the prior art and can be used for the purposes mentioned. As those skilled in the art well know, many groups used in the prior art for making pro-drugs may be usable for the purpose of increasing or causing hydrolysis and/or other lytic reactions and/or other decomposition processes.

The effector unit(s), the targeting unit(s) and/or the optional units described in points 1-9 above may or may not simultaneously serve more than one function, as is well understood

by those skilled in the art. Thus, for example, a targeting unit may simultaneously be an effector unit or comprise several effector units, or a spacer unit may simultaneously be a linker unit or a charge modifier unit or both, or a stabilizer unit may be an effector unit with properties different from those of another effector unit, and so on. Thus, any unit(s) may in principle act as a unit of any other type or as part of any type of unit as well. Also, an effector unit may, for example, have several similar or even completely different functions (e.g., it may for example have therapeutic as well as diagnostic functions, or it may have applications in several fields of diagnostic imaging, or it may be suitable for both imaging purposes and for *in vitro* diagnostics, and so on.)

One or more targeting unit(s) and/or effector unit(s) and/or unit(s) mentioned above in points 1-9 may also be linked to one or more identical, similar and/or different unit(s) directly (without any linker unit(s)) by any type(s) of chemical bond(s), including covalent bonds, coordination bonds, and ionic bonds, and also weaker interactions such as hydrogen bonds, hydrophobic interactions, π-interactions and van der Waals forces, if they in combination with similar and/or different interactions and/or stronger bonds or alone suffice to essentially retain the units linked to each other. If the structure(s) of the units to be linked and/or the need for structural flexibility and/or avoidance of crowding/steric hindrance does not require a linker unit, direct linking is often preferred, as is understood by those skilled in the art.

In one preferred embodiment of the invention, the tumor targeting agent(s) comprise(s) more than one different effector units. In that case, the effector units may be, for example, diagnostic and/or therapeutic units. Thus, for example, it is preferred to use, for boron neutron capture therapy, such agents whose effector units, in addition to comprising boron atoms, also can be detected and/or quantified in the patient *in vivo* after administration of the agent, in order to be able to ascertain that the agent has accumulated adequately in the tumor to be treated, or to optimize the timing of the neutron treatment, and so on. This goal may be achieved e.g. by using such a targeting agent according to the invention that comprise(s) such an effector unit or such effector units that comprise(s) boron atoms (preferably isotope-enriched boron) and also atoms/groups that can be easily detected and/or quantified e.g. by NMRI. Likewise, the presence of more than one type of therapeutically useful effector units may also be preferred. In addition, of course, the targeting units and/or targeting agents may, if desired, be used in combination with one or more "classical" or other tumor therapeutic modalities such as surgery, chemotherapy, other targeting modalities, radiotherapy, immunotherapy etc.

The present invention also relates to diagnostic compositions comprising an amount of one or more of the targeting agents and/or targeting unit(s) of the invention. The diagnostic compositions comprise the present targeting agents and/or targeting unit(s) and optionally one or more diagnostically acceptable carrier(s), solvent(s), vehicle(s), suspending agent(s), labelling agent(s) and/or other additive(s) and/or related material(s). The diagnostic

composition(s) according to the present invention can be used in diagnosing tumors, tumor cells and/or metastases and/or other neoangiogenic disease(s) and/or condition(s). The diagnostic compositions comprise the active component(s) in one or more liquid phase(s), solid phase(s), gel and/or other phase(s), preferably an aqueous phase, in a concentration of about 0.00001 µg/l to 25 x 10^7 µg/l. The compositions may comprise one or more stabilizing agent(s) and/or detergent(s), such as polysorbate(s) and/or Tween, and/or other additives. The concentrations of these other components can be about 0 to 99.9999999 % of the weight of the composition. The diagnostic compositions may be used *in vivo* and/or *in vitro*.

The present invention also relates to pharmaceutical compositions comprising an amount of one or more of the inventional targeting agent(s) and/or targeting unit(s). The pharmaceutical compositions comprising the targeting agent(s) and/or targeting unit(s) according to the invention may be used systemically, non-systemically, locally and/or topically etc., and may be administered by any (one or more) routes, parenterally as well as non-parenterally, e.g. subcutaneously, intravenously, intramuscularly, perorally, intranasally, by pulmonary aerosol, by injection or infusion into a specific organ and/or region, buccally, intracranically, intraperitoneally, etc. or in depot form and so on. The composition(s) may also include any potential combinations of the targeting agent(s) and/or targeting unit(s) with one or more labelling agent(s), imaging agent(s), drug(s) and/or other additives, chemicals and/or substances. The pharmaceutical compositions may be used *in vivo* and/or *in vitro*.

The targeting unit(s) and/or targeting agent(s) and/or pharmaceutical compositions of the present invention may also be used as targeting devices for delivery of DNA and/or RNA and/or structural and/or functional analogues thereof (such as phosphorothioates), and/or related substances, and/or peptide nucleic acids (PNA) and/or their like, and so on, into tumors and/or their metastases and/or the vicinity of such and/or other neoangiogenic tissue(s) and/or organ(s), and/or to isolated cells and/or organ(s) and the like *in vitro*; i.e. as tools for gene therapy and/or related techniques/treatments both *in vivo* and *in vitro*. In such cases the targeting agent(s)and/or targeting unit(s) may or may not be part(s) of viral capsids and/or envelopes, of liposomes and/or of other "containers" of DNA and/or RNA and/or related substances, and/or may be directly coupled/linked/adhered/bonded/bound to the DNA and/or RNA and/or other molecule(s) mentioned above.

Pharmaceutical compositions suitable for peroral use and/or for intravenous injection and/or infusion and/or for other (e.g. local) infusion and/or injection are particularly preferred.

The preparations may be lyophilized and reconstituted before administration or may be stored for example as a solution, solutions, suspensions, suspension-solutions etc. ready for administration or in any form or shape in general, including powders, concentrates, frozen liquids, and any other types. They may also consist of separate entities to be mixed and, possibly, otherwise handled and/or treated etc. before use. Liquid formulations provide the

advantage that they can be administered without reconstitution. The pH of the solution product is in the range of about 1 to about 12, preferably close to physiological pH. The osmolality of the solution can be adjusted to a preferred value using for example sodium chloride and/or sugars, polyols and/or amino acids and/or similar components. The compositions may comprise the active component(s) in a concentration of, generally, about 0.00001 µg/l to 250 g/l, preferably about 0,001 µg/l to 50 g/l, most preferably 0,01 µg/l to 20 g/l. The compositions can further comprise one or more pharmaceutically acceptable excipient(s) and/or stabilizer(s), such as albumin, sugars and/or various polyols, as well as any acceptable additive(s), and/or also any other active ingredient(s) such as prior-art and/or novel chemotherapeutic agent(s). The amounts of these components can vary broadly within a range of about 0 to 99.9999999 wt-% of the weight of the composition.

For oral administration it may be necessary or at least peferable to prepare targeting unit(s) and/or targeting agent(s) that
(1) are stable for oral use
(2) are absorbed adequately when used orally.

Such targeting unit(s) and/or targeting agent(s) may be obtained, for example, by
(a) using peptidomimetic and/or peptidyl analogues and/or structures comprising at least one peptidomimetic and/or peptidyl analogue portion or moiety and/or at least one unnatural and/or modified amino acid; and/or
(b) using suitable stabilizer unit(s) and/or charge modifier unit(s) and/or solubility modifier unit(s) and/or lysis modifier unit(s) (such as unit(s) capable of being hydrolyzed that are directly and/or indirectly coupled/linked to one or more absorption enhancer unit(s)) and/or absorption enhancer unit(s) and/or other unit(s).

Also such embodiments of the invention and such products, such targeting units and targeting agents and other products are included in the invention. Many of such targeting units and targeting agents can be considered as examples of substances under the "prodrug" category.

The present invention also includes the use of the targeting agents and/or targeting unit(s) for the manufacture of reagents and the like for tumor and/or metastasis and/or neoangiogenic condition and/or disease and/or diagnosis and/or for research purposes.

The present invention also includes the use of the targeting agent(s) and/or targeting unit(s) for the manufacture of the above-mentioned diagnostic and/or pharmaceutical compositions for the treatment and targeting of tumors, tumor cells and/or tumor vasculature and/or any neoangiogenic disease(s), condition(s) and/or tissue(s). The targeting units(s) and/or agent(s) can be employed in pharmaceutical compositions to treat cancer(s) as well as other conditions, by administering an effective dose of the targeting agent(s) and/or targeting units(s) or of one or more therapeutically acceptable salt and/or ester and/or other derivative

thereof as such and/or in a pharmaceutical carrier. Therapeutic concentrations or amounts may be determined empirically by testing the targeting agent(s) and/or targeting units(s) in known or novel *in vitro* and/or *in vivo* test systems. Dosages for humans and/or animals may then be obtained and/or extrapolated and/or estimated from these experiments. The targeting targeting unit(s) and/or agent(s) can be administered with or without a pharmaceutically acceptable carrier e.g. at dosages of from about 0.000001 µg to about 40 mg per kg of body weight for example daily and/or as a bolus etc. The composition(s) may be administered systemically, non-systemically, locally and/or topically etc., and by any (one or more) routes, parenterally as well as non-parenterally, e.g. subcutaneously, intravenously, intramuscularly, perorally, intranasally, by pulmonary aerosol, by injection or infusion into a specific organ and/or region, buccally, intracranically, intraperitoneally, etc or in depot form and so on and/or *in vitro*.

The present invention includes also kits and components for kits for diagnosing cancer and/or metastases and/or tumor cells and/or neoangiogenic disease(s) and/or condition(s) *in vivo* and/or *in vitro*. Such kits comprise one or more of the targeting agent(s) and/or targeting units(s) of this invention together with one or more diagnostic and/or pharmaceutical entities and/or other adequate component(s). The kit may comprise for example the targeting agent(s) and/or targeting units(s) as such and/or coupled to any or some of many possible units for detection by e.g. immunological methods, radiation or enzymatic methods, and so on. All possible such modalities are included in the invention.

Further, the targeting unit(s) and/or agent(s) of this invention as well as their motif(s) and sequence(s) can be used as lead compounds to design peptidomimetics for any of the purposes described above.

Yet further, the targeting unit(s) and/or agent(s) as well as the motif(s) and/or sequence(s) of the present invention as such and/or as coupled to and/or entrapped into and/or bound and/or adsorbed onto other material(s) and so on, can be used for the isolation and/or purification and/or identification of the cellular, molecular and/or related biological target(s) of the targeting unit(s) and/or agent(s) of the invention.

Furthermore, the targeting units(s) and/or targeting agent(s) can be used as immunogen(s) and/or antigen(s) for the production of polyclonal and/or monoclonal antisera and/or antibodies *in vivo* and/or poly- and/or monoclonal antibodies *in vitro* and/or *in vivo*.

The following non-limiting examples illustrate the invention further.

Examples

For the following examples commercial reagent suppliers employed are:

Applied Biosystems, Warrington, WA1 4SR,United Kingdom

Bachem AG, Hauptstrasse 144, CH-4416 Bubendorf, Switzerland

Calbiochem-Novabiochem,CH-4448 Läufelfingen, Switzerland

Fluka Chemie GmbH, Buchs, Switzerland

Merck KGaA,Darmstadt,Germany

PE Biosystems,Warrington,United Kingdom

Perseptive Biosystems,Warrington, United Kingdom/Hamburg, Germany

Sigma Aldrich Chemie, Steinheim Germany (also Riedel-deHaën)

Tokyo Kasei Kogyo Co, Ltd., Tokyo, Japan

Bio-Whittaker, Verviers, Belgium

Harlan Laboratories, Horst, The Netherlands

Genset SA, Paris, France

AmershamPharmacia Biotech, Uppsala, Sweden

Qiagen, Hilden, Germany

Terumo, Leuven,Belgium

Vector Laboratories, Burlingame, USA

Example 1

Synthesis of targeting motif/ targeting unit (peptide) IRE. The use of a peptide synthesis resin with no amino acid residue pre-coupled to it, and derivatization of such a resin with a protected amino acid derivative (residue).

The synthesis of the targeting motif/ targeting unit (peptide) IRE (isoleucyl-arginyl-glutamine) was performed by using the manual solid-phase peptide synthesis technique that is described in detail in Example 2 below.

The coupling (binding) of the first amino acid unit (residue) to the hydroxyl groups of a peptide synthesis resin (HMP type; for details, see the listing of materials given below) was carried out by means of the dichlorobenzoyl chloride method as applied to a derivative of L-glutamic acid whose amino function was protected by the 9-fluorenylmethyloxycarbonyl (= FMOC) group and whose "side-chain" carboxyl function (carboxyl group), *i. e.* the carboxyl group that is further away from the amino functionality, was protected as its *tert*-butyl ester (= OtBu). The following protocol was used:

The "empty" resin (resin with no amino acid residue; see below for producer and product number of the commercial resin) was first washed in the shaker described below (in Example 2) with *N,N*-dimethylformamide (DMF; 15 ml of DMF per 1 g of resin) for 20 min and was drained. After addition of five molecular equivalents (relative to the loading capacity of the resin) of the protected L-glutamic acid in DMF, after which 8 equivalents of pyridine were added, followed by shaking for about 3 minutes, without draining. Then, five equivalents of 2,6-dichlorobenzoyl chloride were added, and the mixture was shaken for 18 h at ambient temperature.

After the aforementioned treatment, the resin was drained and washed three times with DMF and dichloromethane as described in the general protocol in Example 2, followed by drying in an argon gas flow. The reagents used this far in the Example were:

HMP Resin
loading capacity: 1.16 mmol/g (as reported by the producer of the commercial product),
Applied Biosystems Cat. No. 400957

Pyridine
Merck Art. No. 9728

Fmoc-L-Glu(OtBu)-OH
CAS No. 71989-18-9
Applied Biosystems Cat. No. GEN911036
Molecular Weight: 425.5 g/mol

From this point on, the synthesis proceeded according to the general method decribed in Example 2. The reagents used in this synthesis, not mentioned above or in Example 2 below, were:

Fmoc-L-Arg(Pbf)-OH

CAS No. 154445-77-9
Applied Biosystems Cat. No. GEN911097
Molecular Weight: 648.8 g/mol

Fmoc-L-Ile-OH
CAS No. 71989-23-6
Perseptive Biosystems Cat. No. GEN911045
Molecular Weight: 353.4 g/mol

The product, IRE, after its isolation and purification according to the general methods described in Example 2, was identified employing MALDI-TOF mass spectral analysis as described in detail in the general protocol below in Example 2.

Identification of the product:
positive mode MALDI-TOF mass spectrum: M+1 ion clearly predominant.

MALDI-TOF data (IRE):
calculated molecular mass = 416.24
observed signals:
417.14 M+H
439.08 M+Na

Example 2

General procedures for peptide synthesis: Manual solid phase syntheses. Mass spectral measurements.

All synthetic procedures were carried out in a sealable glass funnel equipped with a sintered glass filter disc of porosity grade between 2 and 4, a polypropene or phenolic plastic screw cap on top (for sealing), and two PTFE key stopcocks: one beneath the filter disc (for draining) and one at sloping angle on the shoulder of the screw-capped neck (for argon gas inlet).

The funnel was loaded with the appropriate solid phase synthesis resin and solutions for each treatment, shaken powerfully with the aid of a "wrist movement" bottle shaker (Gallenkamp) for an appropriate period of time, followed by filtration effected with a moderate argon gas pressure.

The general procedure of one cycle of synthesis (= the addition of one amino acid unit) was as follows:

The appropriate Wang resin (Applied Biosystems), loaded with approximately 1 mmol of FMOC-peptide (= peptide whose amino-terminal amino group was protected with the 9-fluorenylmethyloxycarbonyl group) consisting of two or more amino acid units, or with approximately 1 mmol of the appropriate FMOC-amino acid (*i.e.*, amino acid carrying the aforementioned protecting group; approximately 2g of resin, 0.5 mmol/g) was treated in the way described below, each treatment step comprising shaking for 2.5 minutes with 30 ml of the solution or solvent indicated and filtration if not mentioned otherwise.

'DCM' means shaking with dichloromethane, and 'DMF' means shaking with *N,N*-dimethylformamide (DMF may be replaced by NMP, *i.e. N*-methylpyrrolidinone).

The steps of the treatment were:

1. DCM, shaking for 10-20 min
2. DMF
3. 20 % (by volume) piperidine in DMF for 5 min
4. 20 % (by volume) piperidine in DMF for 10 min
5. to 7. DMF
8. to 10. DCM
11. DMF
12. DMF solution of 3 mmol of activated amino acid (preparation described below), shaking for 2 hours
13. to 15. DMF
16. to 18. DCM

After the last treatment (18) argon gas was led through the resin for approximately 15 min and the resin was stored under argon (in the sealed reaction funnel if the synthesis was to continue with further units).

Activation of the 9-fluorenylmethyloxycarbonyl-*N*-protected amino acid (FMOC-amino acid) to be added to the amino acid or peptide chain on the resin was carried out, using the reagents listed below, in a separate vessel prior to treatment step no. 12. Thus, the FMOC-amino acid (3 mmol) was dissolved in approximately 10 ml of DMF, treated for 1 min with a solution of 3 mmol of HBTU dissolved in 6 ml of a 0.5 M solution of HOBt in DMF, and then immediately treated with 3 ml of a 2.0 M DIPEA solution for 5 min.

The activation reagents used for activation of the FMOC-amino acid were as follows:

HBTU = 2-(1H-benzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate, CAS No. [94790-37-1], Applied Biosystems Cat. No. 401091, molecular weight: 379.3 g/mol

HOBt = 1-Hydroxybenzotriazole, 0.5 M solution in DMF, Applied Biosystems Cat. No. 400934

DIPEA = N,N-Diisopropylethylamine, 2.0 M solution in N-methylpyrrolidone, Applied Biosystems Cat. No. 401517

The procedure described above was repeated in several cycles using the appropriate different FMOC-amino acids, carrying suitable protecting group(s), to produce a resin-bound source of the appropriate peptide (i.e., a "resin-bound" peptide). The procedure provides also a practical way of connecting certain effector and/or spacer and/or linker units and so on, for instance biotin or the FMOC-Ahx (= 6-(FMOC-amino)-hexanoyl) moiety, to the resin-bound peptide.

Cleavage from the resin was carried out using the following reagent mixture:

trifluoroacetic acid (TFA) 92.5 vol-%
water 5.0 vol-%
ethanedithiol 2.5 vol-%.

After the removal of the protecting FMOC group via steps 1. to 10. (as described in the general procedure above), the resin was treated with three portions of the above reagent mixture (each about 15 ml for 1 g of the resin), each for one hour. The treatments were carried out under argon atmosphere in the way described above. The TFA solutions obtained by filtration were then concentrated under reduced pressure using a rotary evaporator and were recharged with argon. Some diethyl ether was added and the concentration repeated. The concentrated residue was allowed to precipitate overnight under argon in dietyl ether in a refrigerator. The supernatant ether was removed and the precipitate rinsed with diethyl ether. For mass spectrum (MALDI-TOF+) determination, a sample of the precipitate was dissolved in solvents adequate for the spectral method, followed by filtration and, as needeed, dilution of the filtered solution. Further purification was done using reversed phase high-performance liquid chromatographic (HPLC) methods by means of a "Waters 600" pump apparatus using a C-18 type column of particle size 10 micrometers and a linear eluent gradient whose composition was changed during 30 minutes from 99.9% water/0.1% TFA to 99.9% acetonitrile/0.1% TFA. The dimensions of the HPLC columns were 25 cm x 21.2 mm (Supelco cat. no. 567212-U) and 15 cm x 10 mm (Supelco cat. no. 567208-U). Detection was based on absorbance at 218 nm and was carried out using a "Waters 2487" instrument.

The cleavage mixture described above also simultaneously removed the following protecting groups: trityl (Trt) as used for cysteine -SH protection; 2,2,4,6,7-pentamethyldihydrobenzofuran-5-sulfonyl (Pbf) as used for protection of side chain of arginine; the *tert*-butyl group (as an ester group on the carboxyl function; OtBu) as used for

protection of the side-chain carboxyl group of glutamic acid and/or aspartic acid, and can normally be used also for removal of these protecting groups on analogous structures (thiol, guanyl, carboxyl). It did not cause FMOC removal.

The cleavage procedure described above can be carried out also without the removal of the FMOC group, to produce the amino terminal *N*-FMOC-derivative of the peptide, or for a peptide linked to an effector unit (comprising no FMOC).

Mass spectral method employed:

Matrix Assisted Laser Desorption Ionization - Time of Flight (MALDI -TOF)

Type of the intrument:
Bruker Biflex MALDI TOF mass spectrometer

Supplier of the instrument:
Bruker Daltonik GmbH
Fahrenheitstrasse 4
D-28359 Bremen
Germany

MALDI-TOF positive ion reflector mode:

External standards:

Angiotensin II and ACTH(18-39)

Matrix:
alpha-cyano-4-hydroxycinnamic acid (saturated solution in aqueous 50% acetonitrile containing 0.1% of trifluoroacetic acid).

The sample, together with the matrix, was dried onto the target plate under a gentle stream of warm air.

MALDI-TOF negative ion reflector mode:

External standards:
cholecystokinin and glucagon

Matrix:
2,4,6-trihydroxyacetophenone (3 mg/ml in 10 mM ammonium citrate in 50% acetonitrile).

The sample, mixed with the matrix, was immediately dried onto the target plate under vacuum.

Sample preparation:

The specimen was mixed at a 10-100 picomol/microliter concentration with the matrix solution as described.

"Shooting" by nitrogen laser at wavelength 337 nm. The voltage of the probe plate was 19 kV in the positive ion reflector mode and -19 kV in the negative ion reflector mode.

General remarks about the spectra (concerning positive ion mode only):

In all cases the M+1 (*i.e.* the one proton adduct $M+H^+$) signal with its typical fine structure based on isotope satellites was clearly predominant. In almost all cases, the M+1 signal pattern was accompanied by a similar but markedly weaker band of peaks at M+23 (Na+ adduct). In addition to the bands at M+1 and M+23, also bands at M+39 (K+ adduct) or M+56 (Fe+ adduct) could be observed in many cases.

In case of substances with a low molecular mass, the 'matrix signals' (signals due to the constituents of the matrix/ 'the ionization environment') have been omitted (*i.e.*, signals at 294 and 380 Da have been omitted).

The calculated molecular mass values reported within synthesis examples correspond to the most abundant isotopes of each element, i.e., the 'exact masses'. The interpretations given for signals are only tentative.

Example 3

General procedures for I_2-promoted cyclization of peptide/targeting unit or targeting agent on resin (for peptides and targeting units and targeting agents comprising cysteines).

The resin (1 g) was swelled on CH_2Cl_2 (15 ml) and stirred for 20 minutes. The solvent was removed by filtration and the resin was treated once with DMF (15 ml) for three minutes. After filtration, the resin-bound peptide (or targeting agent) was treated with iodine (5 molar equivalents) in DMF (10 ml) for 1 hour.

The DMF-iodine solution was removed by filtration and the residue was washed three times with DMF (15 ml) and three times with CH_2Cl_2 (15ml) for 3 minutes each time.

In case that a 'plain' peptide (without the FMOC group) was to be prepared, the FMOC group was removed and the peptide was released from the resin according to the general procedure described in Example 2 and purified by reversed phase HPLC. In the case of targeting agents comprising no FMOC group, the product was released from the resin and purified analogously.

Material used:
Iodine
CAS No.7553-56-2
molecular weight: 253.81
Merck Art. No. 4760

Example 4

Synthesis of targeting unit (peptide) CIRECG. Inclusion of a spacer group (shows also how spacer or related groups can be utilized for synthetic cost reduction, and to give a targeting peptide whose carboxy-terminal end comprises a spacer unit to which an effector unit can be linked at a distance from the targeting unit, if desired).

Cyclization of targeting unit.

Storage of product in protected and resin-bound form till use for further syntheses.

Preparation of a specifically protected targeting unit (FMOC-CIRECG, *i.e.* CIRECG with a FMOC group at its amino-terminal amino group).

Resin as potential protecting unit.

A) Resin-bound protected peptide. Cyclization.

The resin-bound (fully protected) targeting peptide CIRECG was synthesized using manual synthesis as described in Example 2 above, using a Wang resin pre-loaded with FMOC-glycine and the FMOC-protected amino acids listed below under 'Materials used'. After synthesis, the product carried side-chain protecting groups as follows: trityl (Trt) on each of the two cysteines, 2,2,4,6,7-pentamethyldihydrobenzofuran-5-sulfonyl (Pbf) on the arginine, *tert*-butyl ester (OtBu) on the glutamic acid, and FMOC on the amino-terminal amino group. The carboxy-terminal glycine was included in the compound as a spacer group (not needed for targeting) and in order to decrease costs (no need to use an expensive resin with pre-loaded protected cysteine).

After the last cycle of the coupling process, the resin was shaken for one hour under argon with a DMF solution containing a five-fold excess of iodine (E. Merck, Art. No.4760,

molecular weight 253.81), as described in Example 3, for cyclization of the product (formation of a cystine unit from two cysteine residues).

The resin-bound protected peptide can be used for example in one or more of the following ways:

1. As such as a starting material for the synthesis of the free peptide, as described below.
2. As such as a starting material for the synthesis of the FMOC-protected peptide, as described below.
3. As such as a starting material for further syntheses of targeting units and/or agents, and so on.
4. As a storage form of the free and/or FMOC-protected peptide.

Materials used:

Fmoc-Gly Resin
Applied Biosystems Cat. No. 401421
0.65 mmol/g

Fmoc-L-Cys(trt)-OH
CAS No. 103213-32-7
Applied Biosystems Cat. No. GEN911027
Molecular Weight: 585.7 g/mol

Fmoc-L-Glu(OtBu)-OH
CAS No. 71989-18-9
Applied Biosystems Cat. No. GEN911036
Molecular Weight: 425.5 g/mol

Fmoc-L-Arg(Pbf)-OH
CAS No. 154445-77-9
Applied Biosystems Cat. No. GEN911097
Molecular Weight: 648.8 g/mol

Fmoc-L-Ile-OH
CAS No. 71989-23-6
Perseptive Biosystems Cat. No. GEN911045
Molecular Weight: 353.4 g/mol

Fmoc-L-Cys(trt)-OH as above (again)

B) FMOC-CIRECG.

A small sample of the resin (comprising the still fully protected cyclized peptide) was treated, in a separate vessel, for three hours with the cleavage mixture described in Example 2, in order to cleave the side-chain protecting groups and to cleave the product from the resin. The amino-terminal FMOC group was not removed (steps 1-10 of Example 2 being thus omitted). Then, the product (FMOC-CIRECG) was identified with the aid of its positive mode MALDI-TOF mass spectrum, in which the M+1 ion of FMOC-CIRECG was clearly predominant. Thus, a targeting unit carrying an amino-terminal FMOC group was obtained. This product can be used for further syntheses (of, for example, other targeting units and/or targeting agents) and/or it can be used as such if *N*-protection is considered necessary or advantageous for the specific application in question. - When this product is needed in larger quantities, the whole of the resin carrying the product is advantageously treated as described herein.

The product, FMOC-CIRECG, can also be considered as a targeting agent and/or prototype of such (and the FMOC group thus as an effector unit), the FMOC unit for example being much more facile to detect by a some methods than is a peptide alone.

Identification of the FMOC-protected product:
positive mode MALDI-TOF mass spectrum: M+1 ion clearly predominant.

MALDI-TOF data (FMOC-CIRECG, cyclic):

calculated molecular mass = 899.33

observed signals:
900.39 M+H
922.39 M+Na
938.34 M+K
957.38 M+Fe

C) Targeting unit CIRECG ('free' peptide CIRECG).

The synthesis of the targeting unit CIRECG (*i.e.*, an unprotected peptide) is carried out as follows: The resin carrying the still fully protected product (bound still to the resin) after the synthesis (as described above), or an aliquot thereof, is subjected to the treatment described in Example 2 for FMOC removal (steps 1-10 in that Example), after which the peptide is cleaved from the resin and isolated and purified as described in the same Example. If the cyclic form (comprising cystine) is desired, it is possible and probably advantageous to cyclize the product (for example according to Example 3) before FMOC removal and removal of other protecting groups and cleavage of product from the resin.

Alternatively, the 'free' peptide can prepared by using the FMOC-CIRECG (prepared for example according to point B herein) as starting material and treating the latter with piperidine in solution and isolating and purifying the peptide for example with the aid chromatography, but this is usually not advantageous.

Example 5

Synthesis of resin-bound protected targeting unit (peptide) GCIRECG. Inclusion of two spacer groups (to show how spacer or related groups can be utilized for synthetic cost reduction, and to give a targeting peptide whose carboxy-terminal end and amino-terminal end comprise each a spacer group, to either one or both of which an effector unit or effector units and/or other unit(s) can be linked at a distance from the targeting unit, if desired).

The targeting peptide CIRECG was prepared as described in Example 4, without removing the FMOC group and other protecting groups and without cleaving the product from the resin. The FMOC-CIRECG-resin thus obtained was treated according to the general method described in Example 2. For the addition of the amino-terminal glycine unit, the resin was thus treated with FMOC-glycine (FMOC-Gly-OH), CAS No. [29022-11-5], Novabiochem Cat. No. 04-12-1001, molecular weight: 297.3 g/mol.

The product was preserved in the resin-bound protected (fully protected, no groups removed) form for future targeting agent synthesis, and was used for the synthesis described in Example 6. Identification can be based on the results of that Example.

Example 6

Synthesis of targeting agent [targeting unit CIREC, two spacer units (glycines, one of which can be regarded as a linker unit, too), linked to an effector unit (diethylenetriaminepentaacetic acid minus one OH)].

The following materials were employed:

Diethylenetriaminepentaacetic dianhydride
CAS No. [23911-26-4]
molecular weight: 357.32
Aldrich cat. no. 28,402-5

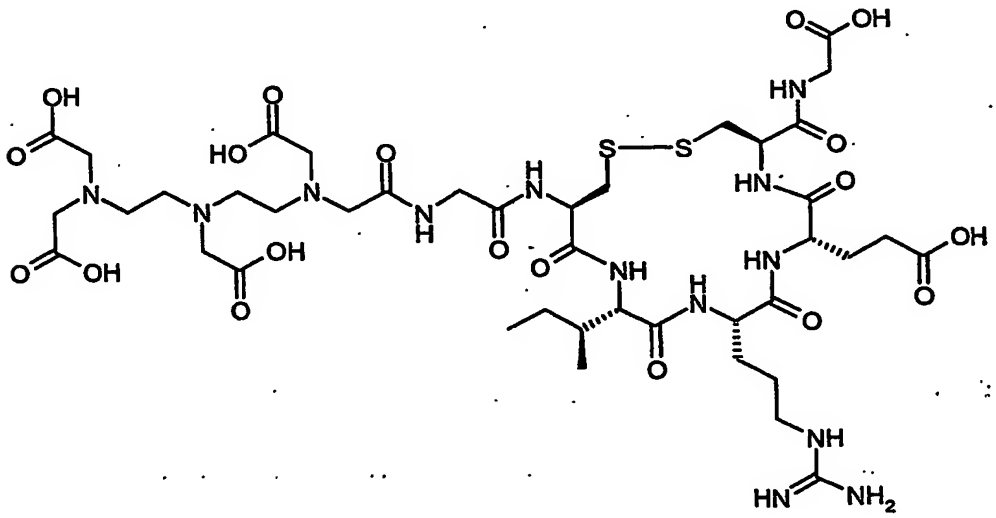
N,N-Dimethylformamide; DMF
peptide synthesis grade

The resin-bound protected peptide FMOC-GCIRECG was prepared as described in Example 5 and the FMOC group was removed as desribed in Example 2 (steps 1-11) but the peptide was not cleaved from the resin.

140 mg of the above dianhydride (5 equivalents) were allowed to soak in 2 ml of DMF overnight. The resin carrying 0.4 mmol of peptide (1 equivalent) was combined with the DMF slurry of the dianhydride (a major part of the dianhydride had obviously dissolved before this) and shaken with the bottle shaker under an atmosphere of argon for 7 hours.

After standing overnight under argon, the DMF-slurry was filtered away through a sintered glass disc of porosity grade 2. The resin remaining on the filter disc was transferred into the equipment described for manual solid phase syntheses in Example 2, and was thoroughly washed (shaken) three times with DMF and dichloromethane as desribed in Example 2.

The cleavage of the product from the resin was carried out in the way desribed in Example 2, and finally a product in which the carboxyl functions no longer were part of anhydride structures was obtained. In the product, one terminal carboxyl group is bonded to the *N*-terminal amino group of GCIRECG with an amide bond, the other ones being free carboxyl groups:



This targeting agent can be used to bind metal ions ['natural' metal ions at a tumor site, or for example radioactive and/or paramagnetic metal ions administered for example systemically via blood to the organism for therapeutic and/or diagnostic purposes, or radioactive and/or paramagnetic and/or other metal ions (that may for example be detectable with the aid of electron microscopic elemental analysis and/or by colour reactions, etc.) administered for example to paraffin-embedded or other tissue slices etc. for the purpose of visualizing tumors *in vitro*], and can also be used to inhibit enzymes that comprise a metal ion

susceptible to the effector unit by virtue of the effector unit's chelating properties that are known well by those skilled in the art.

Another use for this product is as starting material of further targeting agents by chelation of paramagnetic metal ions, radioactive metal ions and/or other metal ions, or by reacting the many carboxyl groups.

Identification of the product:
positive mode MALDI-TOF mass spectrum: M+1 ion clearly predominant.

MALDI-TOF data (DTPA-GCIRECG, acyclic):

calculated molecular mass = 1111.43

observed signals:
1112.43 M+H (strong)
1134.42 M+Na (weak)
1150.42 M+K (weak)
1169.52 M+Fe (weak)

Example 7

Synthesis of targeting unit (peptide) CERICG. Inclusion of a spacer group (to show how spacer or related groups can be utilized for synthetic cost reduction, and to give a targeting peptide whose carboxy-terminal end comprises a spacer unit to which an effector unit can be linked at a distance from the targeting unit, if desired).

The synthesis, including deprotections, removal from resin and isolation and purification, was carried out as described in Example 2, employing the same FMOC-glycine resin as in Example 4 and, in the appropriate order (C, I, R, E, C) the same protected amino acids as are described in Example 4.

After the last cycle of the coupling process, the product was cyclized as described in Example 3. After this treatment the peptide was deprotected (FMOC removal) and cleaved from the resin (with simultaneous removal of the other protecting groups) and isolated and purified in the manner indicated in Example 2, starting from step 13.

Identification of the product:
positive mode MALDI-TOF mass spectrum: M+1 ion clearly predominant.

MALDI-TOF data (CERICG, acyclic):

calculated molecular mass = 679,28

observed signal:
680,28 M+H

MALDI-TOF data (FMOC-CERICG, acyclic):
calculated molecular mass = 901.35

observed signals:
902.42 M+H
924.37 M+Na
959.49 M+Fe

Example 8

Synthesis of targeting unit (peptide) CIREC with two spacer units [one glycine and one 6-aminohexanoic acid (Ahx)] linked to it: AhxCIRECG.

The resin-bound targeting unit (peptide) CIRECG was synthesized analogously to Example 4 above using manual synthesis as described in Example 2 above, and the synthesis was continued with one further unit (the spacer, or linker, unit Ahx) in the same way.

After the last cycle of the coupling process, the product (that was still resin-bound and in its fully protected form) was cyclized by shaking the resin for one hour under argon with a DMF solution containing a five-fold excess of iodine (E. Merck, Art. No.4760, molecular weight 253.81).

The following reagents were employed as starting materials (in this order):

Fmoc-Gly Resin
Applied Biosystems Cat. No. 401421
0.65 mmol/g

Fmoc-L-Cys(trt)-OH
CAS No. 103213-32-7
Applied Biosystems Cat. No. GEN911027
Molecular Weight: 585.7 g/mol

Fmoc-L-Glu(OtBu)-OH
CAS No. 71989-18-9
Applied Biosystems Cat. No. GEN911036
Molecular Weight: 425.5 g/mol

Fmoc-L-Arg(Pbf)-OH
CAS No. 154445-77-9
Applied Biosystems Cat. No. GEN911097
Molecular Weight: 648.8 g/mol

Fmoc-L-Ile-OH
CAS No. 71989-23-6
Perseptive Biosystems Cat. No. GEN911045
Molecular Weight: 353.4 g/mol

Fmoc-L-Cys(trt)-OH as above (again)

Fmoc-6-aminohexanoic acid (Fmoc-6-Ahx-OH)
CAS No. 88574-06-5
Novabiochem Cat. No. 04-12-1111 A22837
Molecular Weight: 353.4 g/mol

The 'free' product AhxCIRECG (product without FMOC and without any other protecting groups, and cleaved from the resin) was prepared as follows: The resin carrying the still fully protected product (bound still to the resin) after the synthesis (as described above) was subjected to the treatment described in Example 2 for FMOC removal (steps 1-10 in that Example), after which the peptide was cleaved from the resin (with concomitant deprotection) and isolated and purified as described in the same Example.

Identification of the product:
positive mode MALDI-TOF mass spectrum: M+1 ion clearly predominant.

MALDI-TOF data (AhxCIRECG, cyclic):

calculated molecular mass = 790.35

observed signals:
791.41 M+H
813.33 M+Na
848.40 M+Fe

Example 9

Synthesis of targeting unit (peptide) IQLRDWGFIL.

The amino-terminally FMOC-protected targeting unit (protected peptide) FMOC-IQLRDWGFIL (comprising targeting motif LRD) was synthesized using manual synthesis as described in Example 2 above.

After the last cycle of the coupling process, a small sample of the resin (containing the still fully protected peptide) was treated, in a separate vessel, for three hours with the cleavage mixture described in Example 2, in order to cleave the side-chain protecting groups and to cleave the product from the resin. The amino-terminal FMOC group was not removed (steps 1-10 of Example 2 being thus omitted). Then, the product (FMOC-IQLRDWGFIL) was identified with the aid of its positive mode MALDI-TOF mass spectrum, in which the M+1 ion of FMOC-IQLRDWGFIL was clearly predominant. Thus, a targeting unit carrying an amino-terminal FMOC group was obtained. This product can be used for further syntheses (of, for example, other targeting units and/or targeting agents) and/or it can be used as such if *N*-protection is considered necessary or advantageous for the specific application in question. - When this product is needed in larger quantities, the whole of the resin carrying the product is advantageously treated as described herein.

The FMOC-protected product can also be considered as a targeting agent and/or prototype of such (and the FMOC group thus as an effector unit).

The following reagents were employed as starting materials (in this order):
Fmoc-Leu Resin
Applied Biosystems Cat. No. 401424
0.77 mmol/g

Fmoc-L-Ile-OH
CAS No. 71989-23-6
Perseptive Biosystems Cat. No. GEN911045
Molecular Weight: 353.4 g/mol

Fmoc-L-Phe-OH
CAS No. 35661-40-6
Applied Biosystems Cat. No. GEN911058
Molecular Weight: 387.4 g/mol

FMOC-Gly-OH
CAS No. 29022-11-5
Novabiochem Cat. No. 04-12-1001
Molecular Weight: 297.3 g/mol

Fmoc-L-Trp(tBoc)-OH
CAS No. 143824-78-6

Applied Biosystems Cat. No. GEN911092
Molecular Weight: 526.6 g/mol

Fmoc-L-Asp(OtBu)-OH
CAS No. 71989-14-5
Perseptive Biosystems Cat. No. GEN911021
Molecular Weight: 411.5 g/mol

Fmoc-L-Arg(Pbf)-OH
CAS No. 154445-77-9
Applied Biosystems Cat. No. GEN911097
Molecular Weight: 648.8 g/mol

Fmoc-L-Leu-OH
CAS No. 35661-60-0
Applied Biosystems Cat. No. GEN911048
Molecular Weight: 353.4 g/mol

Fmoc-L-Gln-OH
CAS No. 71989-20-3
Applied Biosystems Cat. No. GEN911033
Molecular Weight: 368.4 g/mol

Fmoc-L-Ile-OH as above (again)

The 'free' product IQLRDWGFIL (the product without FMOC and without any other protecting groups, and cleaved from the resin) was prepared as follows: The resin carrying the still fully protected product (bound still to the resin) after the synthesis (as described above) was subjected to the treatment described in Example 2 for FMOC removal (steps 1-10 in that Example), after which the peptide was cleaved from the resin (with concomitant deprotection) and isolated and purified as described in the same Example.

Identification of the product:
positive mode MALDI-TOF mass spectrum: M+1 ion clearly predominant.

MALDI-TOF data (IQLRDWGFIL):

calculated molecular mass = 1259.70

observed signals:
1260.7 M+H
1282.6 M+Na

MALDI-TOF data (FMOC-IQLRDWGFIL):
calculated molecular weight = 1481.77

observed signals:
1482.77 M+H
1504.71 M+Na
1526.63 M+K

Example 10

Synthesis of targeting unit (peptide) IQLRD.

The amino-terminally FMOC-protected targeting unit (protected peptide) FMOC-IQLRD (comprising targeting motif LRD) was synthesized using manual synthesis as described in Example 2 above.

After the last cycle of the coupling process, a small sample of the resin (containing the still fully protected cyclized peptide) was treated, in a separate vessel, for three hours with the cleavage mixture described in Example 2, in order to cleave the side-chain protecting groups and to cleave the product from the resin. The amino-terminal FMOC group was not removed (steps 1-10 of Example 2 being thus omitted). Then, the product (FMOC-IQLRD) was identified with the aid of its positive mode MALDI-TOF mass spectrum, in which the M+1 ion of FMOC-IQLRD was clearly predominant. Thus, a targeting unit carrying an amino-terminal FMOC group was obtained. This product can be used for further syntheses (of, for example, other targeting units and/or targeting agents) and/or it can be used as such if *N*-protection is considered necessary or advantageous for the specific application in question. - When this product is needed in larger quantities, the whole of the resin carrying the product is advantageously treated as described herein.

The FMOC-protected product can also be considered as a targeting agent and/or prototype of such (and the FMOC group thus as an effector unit).

The following reagents were employed as starting materials (in this order):

Fmoc-Asp(OtBu) Resin
Applied Biosystems Cat. No. 401417
0.67 mmol/g

Fmoc-L-Arg(Pbf)-OH
CAS No. 154445-77-9

Applied Biosystems Cat. No. GEN911097
Molecular Weight: 648.8 g/mol

Fmoc-L-Leu-OH
CAS No. 35661-60-0
Applied Biosystems Cat. No. GEN911048
Molecular Weight: 353.4 g/mol

Fmoc-L-Gln-OH
CAS No. 71989-20-3
Applied Biosystems Cat. No. GEN911033
Molecular Weight: 368.4 g/mol

Fmoc-L-Ile-OH
CAS No. 71989-23-6
Perseptive Biosystems Cat. No. GEN911045
Molecular Weight: 353.4 g/mol

The 'free' product IQLRD (the product without FMOC) is prepared as follows: The resin carrying the still fully protected product (bound still to the resin) after the synthesis (as described above), or an aliquot thereof, is subjected to the treatment described in Example 2 for FMOC removal (steps 1-10 in that Example), after which the peptide is cleaved from the resin and isolated and purified as described in the same Example.

Identification of the FMOC-protected product:
positive mode MALDI-TOF mass spectrum: M+1 ion clearly predominant.

MALDI-TOF data (FMOC-IQLRD):

calculated molecular mass = 865.43

observed signals:
866.51 M+H
888.47 M+Na

Example 11

Synthesis of targeting unit (peptide) LRELSMGYFK.

The amino-terminally FMOC-protected targeting unit (protected peptide) FMOC-LRELSMGYFK (comprising targeting motif LRE) was synthesized using manual synthesis as described in Example 2 above.

After the last cycle of the coupling process, a small sample of the resin (containing the still fully protected cyclized peptide) was treated, in a separate vessel, for three hours with the cleavage mixture described in Example 2, in order to cleave the side-chain protecting groups and to cleave the product from the resin. The amino-terminal FMOC group was not removed (steps 1-10 of Example 2 being thus omitted). Then, the product (FMOC-LRELSMGYFK) was identified with the aid of its positive mode MALDI-TOF mass spectrum, in which the M+1 ion of FMOC-LRELSMGYFK was clearly predominant. Thus, a targeting unit carrying an amino-terminal FMOC group was obtained. This product can be used for further syntheses (of, for example, other targeting units and/or targeting agents) and/or it can be used as such if *N*-protection is considered necessary or advantageous for the specific application in question. - When this product is needed in larger quantities, the whole of the resin carrying the product is advantageously treated as described herein.

The FMOC-protected product can also be considered as a targeting agent and/or prototype of such (and the FMOC group thus as an effector unit).

The following reagents were employed as starting materials (in this order):

Fmoc-Lys(Boc) Resin
Applied Biosystems Cat. No. 401425
0.70 mmol/g

Fmoc-L-Phe-OH
CAS No. 35661-40-6
Applied Biosystems Cat. No. GEN911058
Molecular Weight: 387.4 g/mol

Fmoc-L-Tyr(tBu)-OH
CAS No. 71989-38-3
Applied Biosystems Cat. No. GEN911068
Molecular Weight: 459.5 g/mol

FMOC-Gly-OH
CAS No. 29022-11-5
Novabiochem Cat. No. 04-12-1001
Molecular Weight: 297.3 g/mol

Fmoc-L-Met-OH
CAS No. 71989-28-1
Applied Biosystems Cat. No. GEN911054

Molecular Weight: 371.5 g/mol

Fmoc-L-Ser(tBu)-OH
CAS No. 71989-33-8
Perseptive Biosystems Cat. No. GEN911062
Molecular Weight: 383.4 g/mol

Fmoc-L-Leu-OH
CAS No. 35661-60-0
Applied Biosystems Cat. No. GEN911048
Molecular Weight: 353.4 g/mol

Fmoc-L-Glu(OtBu)-OH
CAS No. 71989-18-9
Applied Biosystems Cat. No. GEN911036
Molecular Weight: 425.5 g/mol

Fmoc-L-Arg(Pbf)-OH
CAS No. 154445-77-9
Applied Biosystems Cat. No. GEN911097
Molecular Weight: 648.8 g/mol

Fmoc-L-Leu-OH as above (again)

The 'free' product LRELSMGYFK (the product without FMOC and without any other protecting groups, and cleaved from the resin) was prepared as follows: The resin carrying the still fully protected product (bound still to the resin) after the synthesis (as described above) was subjected to the treatment described in Example 2 for FMOC removal (steps 1-10 in that Example), after which the peptide was cleaved from the resin (with concomitant deprotection) and isolated and purified as described in the same Example.

Identification of the product:
positive mode MALDI-TOF mass spectrum: M+1 ion clearly predominant.

MALDI-TOF data (LRELSMGYFK):

calculated molecular mass = 1242.64

observed signals:
1243.35 M+H
1265.31 M+Na

MALDI-TOF data (FMOC-LRELSMGYFK):

calculated molecular mass = 1464.71

observed signals:
1465.40 M+H
1487.43 M+Na
1503.41 M+K

Example 12

Synthesis of targeting unit (peptide) LRELS.

The amino-terminally FMOC-protected targeting unit (protected peptide) FMOC-LRELS (comprising targeting motif LRE) was synthesized using manual synthesis as described in Example 2 above.

After the last cycle of the coupling process, a small sample of the resin (containing the still fully protected cyclized peptide) was treated, in a separate vessel, for three hours with the cleavage mixture described in Example 2, in order to cleave the side-chain protecting groups and to cleave the product from the resin. The amino-terminal FMOC group was not removed (steps 1-10 of Example 2 being thus omitted). Then, the product (FMOC-LRELS) was identified with the aid of its positive mode MALDI-TOF mass spectrum, in which the M+1 ion of FMOC-LRELS was clearly predominant. Thus, a targeting unit carrying an amino-terminal FMOC group was obtained. This product can be used for further syntheses (of, for example, other targeting units and/or targeting agents) and/or it can be used as such if *N*-protection is considered necessary or advantageous for the specific application in question. - When this product is needed in larger quantities, the whole of the resin carrying the product is advantageously treated as described herein.

The FMOC-protected product can also be considered as a targeting agent and/or prototype of such (and the FMOC group thus as an effector unit).

The following reagents were employed as starting materials (in this order):

Fmoc-Ser(tBu) Resin
Applied Biosystems Cat. No. 401429
0.64 mmol/g

Fmoc-L-Leu-OH
CAS No. 35661-60-0
Applied Biosystems Cat. No. GEN911048

Molecular Weight: 353.4 g/mol

Fmoc-L-Glu(OtBu)-OH
CAS No. 71989-18-9
Applied Biosystems Cat. No. GEN911036
Molecular Weight: 425.5 g/mol

Fmoc-L-Arg(Pbf)-OH
CAS No. 154445-77-9
Applied Biosystems Cat. No. GEN911097
Molecular Weight: 648.8 g/mol

Fmoc-L-Leu-OH as above (again)

The 'free' product LRELS (the product without FMOC) is prepared as follows: The resin carrying the still fully protected product (bound still to the resin) after the synthesis (as described above), or an aliquot thereof, is subjected to the treatment described in Example 2 for FMOC removal (steps 1-10 in that Example), after which the peptide is cleaved from the resin and isolated and purified as described in the same Example.

Identification of the FMOC-protected product:
positive mode MALDI-TOF mass spectrum: M+1 ion clearly predominant.

MALDI-TOF data (FMOC-LRELS):

calculated molecular mass = 838.42

observed signals:
839.51 M+H
861.42 M+Na

Example 13

General procedure employed in the syntheses of biotinylated compounds [targeting agents comprising one D-biotin (vitamin H) as an effector unit].

The appropriate protected peptide was synthesized on using solid-phase synthesis according to the general procedure described in Example 2. The peptide was not deprotected and also not removed from the resin. The resin-bound peptide was added to the reaction flask. The resin was swelled using CH_2Cl_2 (15 ml) and stirred for 20 minutes. The solvent was removed by filtration and the resin was treated once with DMF for three minutes. The peptide was deprotected using 20 % piperidine solution in DMF (20ml) and

shaking therewith for 5, and the process was repeated using (now shaking for 10 minutes). The resin was washed three times with DMF (15 ml) and three times with CH_2Cl_2 (15ml) and once with DMF (15 ml) for three minutes each time.

D-biotin (3 molar equivalents) in DMF (10 ml) (heterogenous suspension) was treated in a separate vessel with a 0.5 M solution of HBTU/HOBT in DMF (3 molar eq.) for one minute. Into the vessel was added a 2 M solution of di-isopropylethylamine in NMP (6 molar eq.). After the addition, the reaction mixture became homogenous. The mixture was added to the reaction apparatus and the apparatus was shaken for 2 hours.

The reaction mixture was then filtered and the residue was washed three times with DMF (15 ml) and three times with CH_2Cl_2 (15ml) for 3 minutes each time.

In case that the peptide was to be both biotinylated as described herein and cyclized by an iodine treatment as described in Example 3, the cyclization was performed after the biotinylation procedure.

Material used:

D-Biotin (Vitamin H)
CAS No. 58-85-5
molecular weight: 244.3
Sigma B-4501
99%

Example 14

Synthesis of targeting agent Bio-LRELS (Bio = D-biotin = vitamin H), comprising the effector unit D-biotin coupled (linked directly, without specific linker units) via its carboxyl group to the N-terminal amino group of the peptide LRELS by virtue of an amide bond, and also comprising the targeting unit LRELS.

The targeting agent was synthesized using manual synthesis as described in Example 2 above (analogously to the synthesis in Example 12 above) and using the biotinylation procedure described in Example 13 above as the final coupling step. In this final coupling process, D-biotin was employed instead of a protected amino acid. D-biotin was not protected but was employed as such. The product was isolated and purified in the manner indicated in Example 2 and identified by positive-mode MALDI-TOF spectroscopy (M+1 ion clearly predominant).

The total yield of the synthesis starting from the serine resin all the way up to the HPLC-purified product was 29% (as calculated on the basis of the serine resin using the loading degree reported by the manufacturer of the resin).

Identification of the product:
positive mode MALDI-TOF mass spectrum: M+1 ion clearly predominant.

MALDI-TOF data (Bio-LRELS):

calculated molecular mass = 842.43

observed signal:
843.52 M+H

Example 15

Synthesis of targeting agent Bio-CIRECG (Bio = D-biotin = vitamin H), comprising the effector unit D-biotin coupled (linked directly, without specific linker units) via its carboxyl group to the N-terminal amino group of the peptide CIRECG by virtue of an amide bond, and also comprising the targeting unit CIRECG or the targeting unit CIREC and the spacer unit G.

The targeting agent was synthesized using manual synthesis as described in Example 2 above (analogously to the synthesis in Example 4 above). In the final coupling process, D-biotin was employed instead of a protected amino acid. D-biotin was not protected but was employed as such. The product was isolated and purified in the manner indicated in Example 2 after an iodine-promoted cystine cyclization that was carried out according to the general method described in Example 3.

Identification of the product:
positive mode MALDI-TOF mass spectrum: M+1 ion clearly predominant.

MALDI-TOF data (Bio-CIRECG, cyclic):

calculated molecular mass = 903.34

observed signals:
904.40 M+H
926.32 M+Na
961.45 M+Fe

Example 16

Synthesis of targeting agent Bio-LRELSMGYFK (Bio = D-biotin = vitamin H), comprising the effector unit D-biotin coupled (linked directly, without specific linker units) via its carboxyl group to the N-terminal amino group of the peptide LRELSMGYFK by virtue of an amide bond, and also comprising the targeting unit LRELSMGYFK.

The targeting agent was synthesized, isolated, purified and identified analogously to the procedures in Examples 11 and 14 above.

Identification of the product:
positive mode MALDI-TOF mass spectrum: M+1 ion clearly predominant.

MALDI-TOF data (Bio-LRELSMGYFK):

calculated molecular mass = 1468.72

observed signals:
1469.60 M+H
1491.48 M+K

Example 17

Synthesis of targeting agent Bio-IQLRD (Bio = D-biotin = vitamin H), comprising the effector unit D-biotin coupled (linked directly, without specific linker units) via its carboxyl group to the N-terminal amino group of the peptide IQLRD by virtue of an amide bond, and also comprising the targeting unit IQLRD.

The targeting agent was synthesized, isolated, purified and identified analogously to the procedures in Examples 10 and 14 above.

Identification of the product:
positive mode MALDI-TOF mass spectrum: M+1 ion clearly predominant.

MALDI-TOF data (Bio-IQLRD):

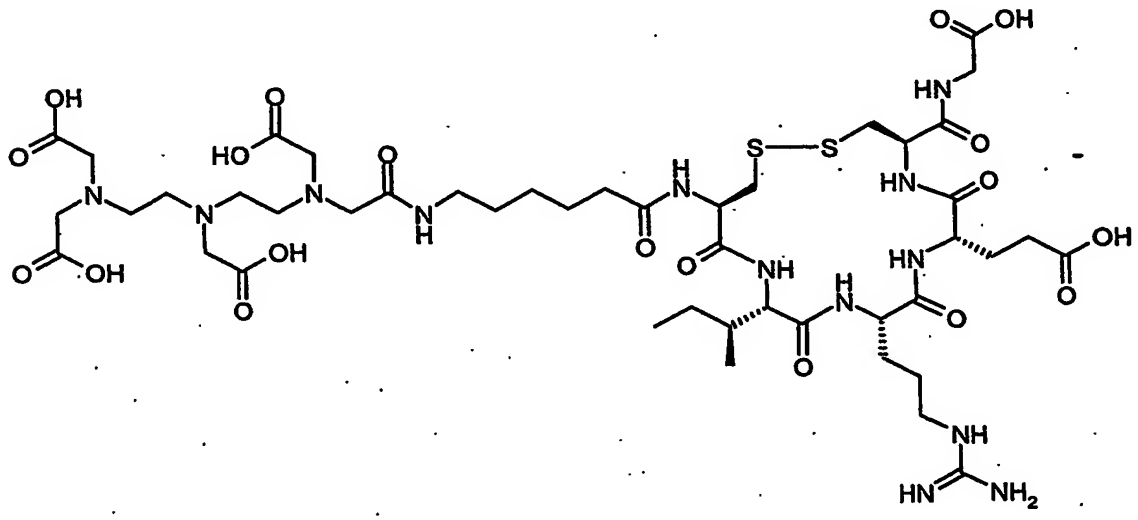
calculated molecular mass = 869.44

observed signal:
870.37

Example 18

Synthesis of targeting agent 'DTPA-AhxCIRECG' [targeting unit (peptide) CIREC with two spacer units (one glycine and one 6-aminohexanoic acid (Ahx) (or: targeting unit AhxCIRECG), linked to an effector unit (diethylenetriaminepentaacetic acid minus one OH)].

The structure of the targeting agent to be synthesized:



FMOC-Ahx-CIRECG resin was prepared (according to what is described in Example 8) and treated with elemental iodine by the methods described in Example 3 and 8, and the protecting FMOC group was removed as described in Example 2, after which the product AhxCIRECG (cyclic by virtue of cystine unit) was cleaved from the resin (with concomitant removal of the other protecting groups) and purified by HPLC according to the general methods described in Examples 2 and 3.

The isolated purified peptide thus obtained was then treated with 10 molecular equivalents of diethylenetriaminepentaacetic dianhydride in the precence of one molecular equivalent of triethylamine in DMF solution (0.01 M solution as calculated on the basis of the peptide) for 18 hours. After this treatment, the volume was doubled by addition of water to the DMF solution, and the solution was put aside and allowed to stay still for 4 hours. Finally, the solvents were evaporated *in vacuo* and the residue was mixed in water containing 0.1% trifluoroacetic acid and was filtered and the filtrate was purified by reversed-phase HPLC. The product was clearly identified by its M+1 peak in the MALDI-TOF mass spectrum.

The following materials were used in the synthesis:

Diethylenetriaminepentaacetic dianhydride
CAS No. 23911-26-4

molecular weight: 357.32
Aldrich 28,402-5
98%

DMF; N,N-Dimethylformamide;
Merck 1.02937
UV-spectral grade

Triethylamine
CAS No. 121-44-8
molecular weight: 101.19
Riedel-de-Haën 16304
99%

Identification of the product:
positive mode MALDI-TOF mass spectrum: M+1 ion clearly predominant.

MALDI-TOF data (DTPA-AhxCIRECG, cyclic):

calculated molecular mass = 1165.47

observed signals:
1166.27 M+H (strong)
1188.24 M+Na (weak)
1223.28 M+Fe (medium)

Example 19

Synthesis of targeting agent 'Gd-DTPA-AhxCIRECG' [targeting unit (peptide) CIREC with two spacer units (one glycine and one 6-aminohexanoic acid (Ahx) (or: targeting unit AhxCIRECG), linked to an effector unit (diethylenetriaminepentaacetic acid minus one OH, chelated to Gd^{3+})].

The targeting agent prepared in Example 18 was chelated with Gd(III) ions as follows:

One molecular equivalent of the chelator described above (in Example 18) was dissolved in 21 molecular equivalents of aqueous 0.01 M ammonium bicarbonate and 7 molecular equivalent of aqueous 0.01 M gadolinium(III) chloride was mixed with it at room temperature. After 16 hours, the mixture was deep-frozen and lyophilized. The residue was dissolved in water and filtered. The product was identified by its negative-ion mode MALDI-TOF mass spectrum, giving the molecular weight 1320.55 g/mol. The isotope pattern typical of Gd was seen in the spectrum.

The following materials were used in the synthesis:

Gadolinium(III) chloride hydrate
CAS No. 19423-81-5
Aldrich 45,085-5
41% Gd

Ammonium bicarbonate
CAS No. 1066-33-7
molecular weight: 79.06
Sigma A-6141
99%

Identification of the product:

MALDI-TOF data (Gd-DTPA-AhxCIRECG, cyclic)
negative ion MALDI-TOF:

calculated molecular mass = 1317.4 (Gd isotope 155)

observed signals:
1316.10 M-1 (Gd-155)
1317
1318
1319 strongest signal M-1 (Gd-158)
1320
1321
1322

Example 20

Synthesis of targeting agent (anthraquinone-2-carbonyl)-CIRECG ('Aqc-CIRECG'; cyclic byu virtue of cystine unit), comprising the effector unit anthraquinone-2-carboxylic acid coupled (linked directly, without specific linker units) via its carboxyl group to the N-terminal amino group of the peptide CIRECG.

The protected uncyclized resin-bound targeting peptide FMOC-CIRECG was prepared as described in Example 4 above, with the exceptions that the cyclization (iodine treatment) and further work-up were postponed to be carried out after the coupling of the effector unit.

The coupling of the effector unit was carried out by means of manual synthesis similar to the one described in Example 2 above, with the exception of step 12, DIPEA and anthraquinone-2-carbonyl chloride being added (instead of a protected amino acid) in a three-fold excess to the resin-bound peptide and without any separate activation steps. DIPEA was added first as a 0.34 M solution in DMF, and anthraquinone-2-carbonyl chloride right after a short shaking, without any draining of the resin, as a 0.034 M solution in DMF followed by shaking for 4 hours.

Material used (in addition to the ones mentioned in Example 4):

Anthraquinone-2-carbonyl chloride
Molecular weight 270.67 g/mol
Tokyo Kasei Cat. No. TCI-GR A0503

Identification of the product:
positive mode MALDI-TOF mass spectrum: M+1 ion clearly predominant.

MALDI-TOF data (Aqc-CIRECG; cyclic):

calculated molecular mass = 912.35

observed signals:
912.39 M+H
934.29 M+Na

Example 21

General method for the cyclization of a peptide and/or targeting unit and/or targeting agent and/or targeting motif and/or targeting motif, and/or part thereof, in the form of a lactam (as macrolactam; by virtue of a peptide bond between lysine and aspartic acid that were included in the sequence at the ends of an 'intermediary' sequence).

The uncyclized, fully protected, resin-bound peptides were prepared manually by means of the general method described in Example 2 above.

Prior to the cyclization, a selective, one-process, dismantling of the side-chain protecting groups of lysine and aspartic acid [the said groups were: 4-methyltrityl on the lysine unit and 2-phenylisopropyl (ester) on the aspartic acid unit] was carried out with diluted TFA (4 % in dichloromethane). The cyclization involved a condensation between the side-chain carboxyl group of the aspartic acid unit and the 6-amino group (side-chain amino group) of the lysine unit. Activation was by a PyAOP/HOAt/DIPEA reagent mixture (for details and abbreviation explanation, see below) or, alternatively, by the HBTU/HOBt/DIPEA mixture

described in Example 2. The equipment, common solvents, and practical techniques were similar to those described in Example 2.

The initially fully protected resin-bound peptide (0.3 mmol) was shaken under argon atmosphere at room temperature with different solutions (about 10 mL) for the periods of time indicated below, followed by filtration:

1. dichloromethane, for 20 min.
2. 4 % (by volume) trifuoroacetic acid in dichloromethane, for 15 min.
3. 0.2 M DIPEA in 1:10 mixture of NMP and dichloromethane, for 3 min.
4. dicloromethane, for 3 min.
5. dicloromethane, for 3 min.
6. dicloromethane, for 3 min.
7. DMF, for 3 min.
8. activation, for 4 hours, according to the description below:

A mixture of PyAOP and HOAt, or alternatively a mixture of HBTU and HOBt, 3 molecular equivalents of both components with respect to the resin-bound peptide (thus, 0.9 mmol both) in DMF (7 mL), was shaken with the resin for 1 min without filtration, followed by addition of 6 molecular equivalents of 2 M DIPEA in NMP.

After step 8 above, the procedures continued as described in Example 2, starting from step 13.

The reagents for activation in this type of cyclization were:

PyAOP = 7-Azabenzotriazol-1-yloxytris(pyrrolidino)phosphonium hexafluorophosphate
CAS No. 156311-83-0
PE Biosystems Cat. No. GEN076531
Molecular Weight: 521.4 g/mol

HOAt = 1-Hydroxy-7-azabenzotriazole
0.5 M solution in DMF
Applied Biosystems Cat. No. 4330631

DIPEA = *N,N*-Diisopropylethylamine
2.0 M solution in *N*-methylpyrrolidinone
Applied Biosystems Cat. No. 401517

For materials in the 'HBTU and HOBt' alternative, see the materials indicated in Example 2.

Starting materials for the 'special' amino acid units (aspartic acid and lysine), between which the 'extra' peptide bond was formed:

Fmoc-Lys(Mtt) Resin
0.68 mmol/g
Bachem Cat. No. D-2565.0005

Fmoc-Asp(2-phenylisopropyl ester)-OH
Molecular weight: 473.53 g/mol
Bachem Cat. No. B-2475.0005

Example 22

Synthesis of targeting unit DIREK (non-cyclized form and cyclized form that is cyclic by virtue of lactam bridge).

Cyclization of targeting unit with lactam bond (lactam bridge; 'extra' amide bond').

Storage of non-cyclic and cyclic product in protected and resin-bound form till use for further syntheses.

Use of protected resin-bound targeting unit for syntheses of targeting agents and of targeting unit carrying a spacer/linker unit.

Preparation of a specifically protected targeting unit [FMOC-DIREK (cyclic by virtue of lactam bridge), *i.e.* DIREK (cyclic by virtue of lactam bridge) with a FMOC group at its amino-terminal amino group].

A 'resinous' analogue of DIREK [resin-bound completely protected non-cyclized DIREK] and further, from it, the cyclic form (macrolactam) of DIREK were prepared by coupling procedures as depicted in Example 2, and (the cyclized form of protected DIREK) by subsequent formation of the amide bridge (*i.e.*, on-resin cyclization) as described in Example 21 above (the 'HBTU and HOBt' alternative in activation step 8.).

In addition to the 'general' reagents mentioned in the above Examples, the following starting materials were employed (in this order):

Fmoc-Lys(Mtt) Resin
0.68 mmol/g
Bachem Cat. No. D-2565.0005

Fmoc-L-Glu(OtBu)-OH

CAS No. 71989-18-9
Applied Biosystems Cat. No. GEN911036
Molecular Weight: 425.5 g/mol

Fmoc-L-Arg(Pbf)-OH
CAS No. 154445-77-9
Applied Biosystems Cat. No. GEN911097
Molecular Weight: 648.8 g/mol

Fmoc-L-Ile-OH
CAS No. 71989-23-6
Perseptive Biosystems Cat. No. GEN911045
Molecular Weight: 353.4 g/mol

Fmoc-Asp(2-phenylisopropyl ester)-OH
Molecular Weight: 473.53 g/mol
Bachem Cat. No. B-2475.0005

The 'resinous' (resin-bound) products prepared can be regarded as storage forms of (*i.e.*, are possible source materials for the preparation of) free (non-protected, 'plain') non-cyclic and cyclic DIREK and/or non-cyclic and cyclic FMOC-DIREK by FMOC-removal (or not) and deprotection and release from resin as described in Example 2. One of them (the cyclized one comprising still the FMOC group) also served as actual starting material of the preparation described in Example 23: cyclic Bio-DIREK. The corresponding non-cyclized one comprising still the FMOC group in turn served as actual starting material of the preparations described in Examples 24-26: cyclic Ahx-DIREK, non-cyclic and cyclic FMOC-Ahx-DIREK, and cyclic DTPA-Ahx-DIREK.

Identification of the FMOC-protected product:
positive mode MALDI-TOF mass spectrum: M+1 ion clearly predominant.

MALDI-TOF data (FMOC-DIREK, cyclic):

calculated molecular mass = 863.42

observed signal:
864.53 M+H

Example 23

Synthesis of targeting agent Bio-DIREK (cyclized form that is cyclic by virtue of lactam bridge).

The 'resinous' source material of Bio-DIREK was prepared by treatment of DIREK resin (prepared as described in Example 22, the cyclized resinous product) with biotin as described in Example 13 (FMOC removal before biotin treatment). The "free" product was obtained by deprotection and release from resin (as described in Example 2), and was isolated, purified and identified as described in Example 2.

Identification of the product:
positive mode MALDI-TOF mass spectrum: M+1 ion clearly predominant.

MALDI-TOF data (Bio-DIREK, cyclic)
calculated molecular mass = 867.43

observed signal:
868.58 M+H

Example 24

Synthesis of cyclic FMOC-protected targeting unit FMOC-Ahx-DIREK (FMOC-protected cyclized form/lactam form/macrolactam form) that also carries the spacer and/or linker unit Ahx. (Can also be considered as a targeting agent by virtue of the FMOC group).

The 'resinous' (resin-bound), protected form of uncyclized DIREK was prepared as described in Example 22. The spacer/linker unit Ahx (6-aminohexanoic acid) that was in its FMOC-protected form [= 6-(FMOC-amino)-hexanoic acid], was coupled to the resin-bound targeting unit (uncyclized DIREK) whose FMOC group had been removed but that was otherwise still fully protected. The general procedure, described in Example 2, was employed, yet without the final FMOC removal after coupling.

Cyclization of Ahx-DIREK was carried out on resin according to the general method described in Example 21 applying the 'PyAOP and HOAt' method variant in activation step 8.

The product was isolated and identified as described in Example 2.

Reagent employed as additional starting material:

Fmoc-6-aminohexanoic acid (Fmoc-6-Ahx-OH)
CAS No. 88574-06-5
Novabiochem Cat. No. 04-12-1111 A22837
Molecular Weight: 353.4 g/mol

Identification of the FMOC-protected product:
positive mode MALDI-TOF mass spectrum: M+1 ion clearly predominant.

MALDI-TOF data (FMOC-Ahx-DIREK, cyclic):

calculated molecular mass = 976.50

observed signal:
977.66 M+H

Example 25

Synthesis of cyclic targeting unit carrying a spacer and/or linker unit (Ahx-DIREK, cyclic by virtue of a lactam bridge). Solution-phase FMOC removal procedure.

The preparation of the title product, carried out in solution, started from the purified cyclic FMOC-Ahx-DIREK, (i.e., from the FMOC-protected but otherwise deprotected targeting unit/agent cleaved from the resin and isolated and purified as described in Example 24). The FMOC-peptide was treated with a piperidine solution (20% by volume) in DMF at room temperature for 10 minutes before immediate evaporation under reduced pressure using gentle warming (rotary evaporator/ 40 °C bath) during 10 minutes. The residue was mixed with a few drops of diethyl ether and, after precipitation, the supernatant ether was drained away. The residue was dissolved in a small amount of a mixture of acetonitrile, methanol and water (1:1:1 by volume), diluted with water to a concentration suitable for HPLC separation, and filtered. The filtrate was purified by using the HPLC apparatus and methodology described in Example 2.

The yield of the purified product was 45%.

Identification of the product:
positive mode MALDI-TOF mass spectrum: M+1 ion clearly predominant.

MALDI-TOF data (Ahx-DIREK, cyclic):

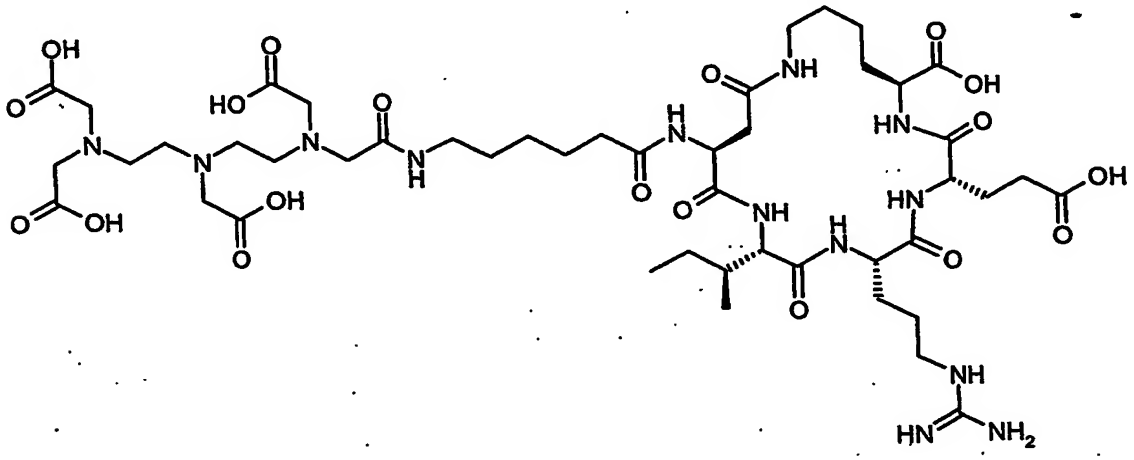
calculated molecular mass = 754.43

observed signal:
755.51 M+H

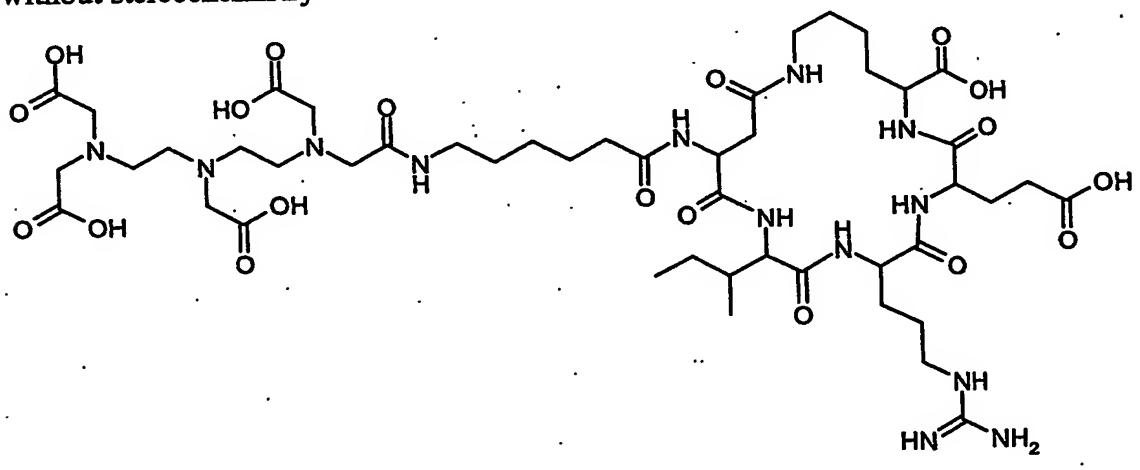
Example 26

Synthesis of targeting agent 'DTPA-Ahx-DIREK' [targeting unit (peptide/ peptidomimetic analogue/peptidyl analogue) DIREK that is cyclic by virtue of a lactam bridge, comprising the targeting motif IRE; one spacer/linker unit (6-aminohexanoic acid = Ahx); or: targeting unit Ahx-DIREK; linked to an effector unit (diethylenetriaminepentaacetic acid (DTPA) minus one OH)].

The structure of the targeting agent synthesized:



without stereochemistry



The starting material for the synthesis of the cyclic (cycliziced) DTPA-Ahx-DIREK (lactam/macrolactam) was a purified sample of cyclic Ahx-DIREK, whose preparation is described in Example 25. It was treated with diethylenetriaminepentaacetic dianhydride in a manner similar to the one described in Example 18 (omitting the first paragraph of the Example).

Identification of the product:
positive mode MALDI-TOF mass spectrum: M+1 ion clearly predominant.

MALDI-TOF data (DTPA-Ahx DIREK, cyclic):

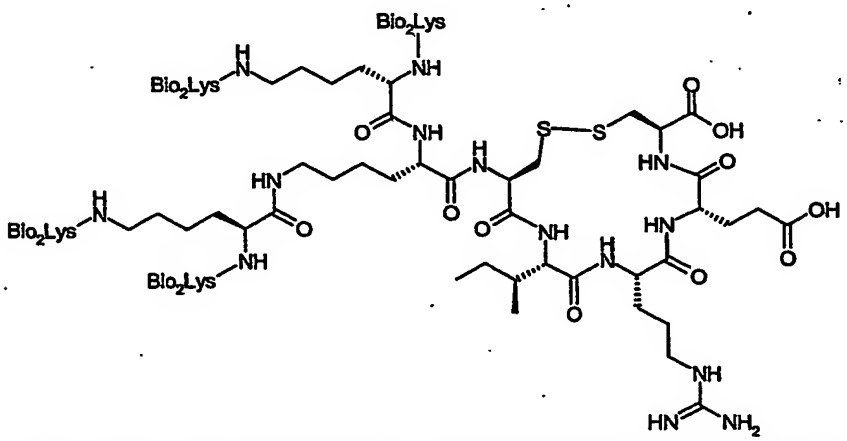
calculated molecular mass = 1129.56

observed signals:
1130.37 M+H
1168.29 M+K
1086.39 M-[COO]+H

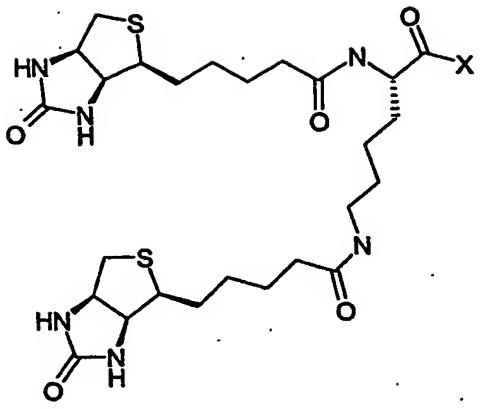
Example 27

Synthesis of targeting agent Bio_8-K_4-K_2-K-CIRECG (cyclic by virtue of cystine; Bio = D-biotin = vitamin H), comprising eight identical effector units D-biotin coupled (linked via a dendrimeric structure that can be considered as seven linker units and/or seven spacer units and/or as one larger spacer and/or linker unit) each via its carboxyl group to one amino group of a lysine residue (unit), either the N-terminal amino group or the side-chain amino group, and the dendrimeric structure (four lysines each carrying two effector biotin units, these lysines being coupled via the carboxyl functions to two further lysines and they in turn to one lysine and this to the amino terminus of the peptide CIRECG by virtue of an amide bond, and also comprising the targeting unit CIRECG (or the targeting unit CIREC and the spacer unit G).

The product has the formula shown below:



Moiety Bio_2Lys has the structure depicted in the formula of Bio_2Lys-X below (X represents the rest of the molecule, not included in the moiety)



and can be stated to comprise an eight-fold biotinylated eight-branch dendrimeric-linker/spacer unit on the N-terminus of CIRECG.

The fully protected resin-bound peptide CIRECG was prepared as described in Example 4. The cyclization by iodine was postponed to be done right before the clevage of the final product from the resin. The dendrimeric K_4-K_2-K- linker structure was conctructed by means of the general coupling methods described in Example 2, so that the sequence CIRECG was continued first with one lysine unit (protected with one FMOC-group on each of its two amino groups). Then, the procedure (lysine addition) was repeated using doubled amounts of coupling reagents and doubly FMOC-protected lysine to couple two more lysine units, one of them on the side-chain amino and one on the amino-terminal amino group. Finally, the procedure was repeated using four-fold amounts of coupling reagents and protected lysine to add still four more FMOC-protected (two FMOC groups on each) lysine units (coupling to all available amino groups).

Biotinylation was done according to the general method described in Example 13 using 24 molecular equivalents of coupling reagents and biotin to the resin-bound dendrimeric peptide to afford a stucture comprising eight biotin units bound to the branched molecule. Cyclization and isolation were then performed in a manner similar to that described in Example 15 by means of the general methods described.

Reagent (in addition to materials described in the above Examples):

Fmoc-L-Lys(Fmoc)-OH
CAS No. 78081-87-5
Molecular weight: 590.7 g/mol
PerSeptive Biosystems Cat. No. GEN911095
Hamburg
Germany

Identification of the product:

positive mode MALDI-TOF mass spectrum: M+1 ion clearly predominant.

MALDI-TOF data (Bio_8-K_4-K_2-K-CIRECG, cyclic):

calculated molecular mass = 3382.55

observed signals:
3383.25 M+H

Example 28

Synthesis of targeting agent Bio-IRE (Bio = D-biotin = vitamin H), comprising the effector unit D-biotin coupled (linked directly, without specific linker units) via its carboxyl group to the N-terminal amino group of the peptide IRE by virtue of an amide bond, and also comprising the targeting unit IRE.

The targeting agent was synthesized, isolated, purified and identified analogously to the procedures in Examples 1 and 14 above.

Identification of the product:
positive mode MALDI-TOF mass spectrum: M+1 ion clearly predominant.

MALDI-TOF data (Bio-IRE):

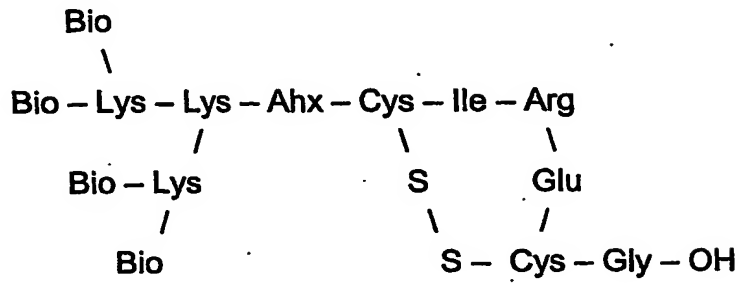
calculated molecular mass = 642.32

observed signal:
643.52 M+H

Example 29

Synthesis of targeting agent Bio_4-K_2-K-AhxCIRECG (cyclic by virtue of cystine; Bio = D-biotin = vitamin H), comprising four identical effector units D-biotin coupled (linked via a dendrimeric structure that can be considered as two plus one plus one linker units and/or spacer units and/or as one larger spacer and/or linker unit) each via its carboxyl group to one amino group of a lysine residue (unit), either the N-terminal amino group or the side-chain amino group, and the dendrimeric structure (two lysines each carrying two effector biotin units, these lysines being coupled via the carboxyl functions to one further lysine and this in turn by virtue of an amide bond to the amino group of one Ahx (6-aminohexanoic acid) and this by virtue of an amide bond to the amino terminus of the peptide CIRECG, and also comprising the targeting unit CIRECG (or the targeting unit CIREC and the spacer unit G).

The product has the formula shown below:



and can be stated to comprise a four-fold biotinylated four-branch linker/spacer unit on the N-terminus of AhxCIRECG.

The synthesis was carried out as follows: The fully protected resin-bound uncyclized targeting unit (peptide with two spacer/linker units) AhxCIRECG was prepared as described in Example 8 above. The cyclization with the aid of iodine was postponed to be done right before the clevage of the final product from the resin. The branched structure comprising the four biotins and the three lysines was conctructed by means of the general coupling methods described in Example 2, so that the sequence AhxCIRECG was continued first with one lysine unit (protected with one FMOC-group on each of its two amino groups). Then, the procedure (lysine addition) was repeated using doubled amounts of coupling reagents and the doubly protected (FMOC groups) lysine, in order to couple two more lysine units, one of them on the side-chain amino and one on the amino-terminal amino group of the first-coupled lysine unit.

Biotinylation was done according to the general method described in Example 13 using 12 molecular equivalents of coupling reagents and biotin, employing the resin-bound branched peptide, to afford a stucture comprising four biotin units. Cyclization and isolation were then performed in a manner similar to that described in Example 15 by means of the general methods described.

Reagent (in addition to the materials described in the above Examples):

Fmoc-L-Lys(Fmoc)-OH
CAS No. 78081-87-5
Molecular weight: 590.7 g/mol
PerSeptive Biosystems Cat. No. GEN911095

Identification of the product:
positive mode MALDI-TOF mass spectrum: M+1 ion clearly predominant.

MALDI-TOF data (Bio_4-K_2-K-AhxCIRECG, cyclic):

calculated molecular mass = 2078.94

observed signal:

2079.85 M+H

Example 30

Synthesis of the D-amino acid analogues/opposite enentiomers/'mirror images' of the products of the previous Examples.

Any one of the products (targeting units, targeting motifs, targeting agents and protected, resin-bound, FMOC-protected substances, and any others) can be prepared in exactly similar fashion as those described in any one of the previous Examples, as the corresponding D-series analogues (comprising in all cases a D-amino acid or unnatural amino acid or a derivative/protected form/activated form etc. of such, instead of the L-one or a derivative/protected form/activated form etc. of such, and more generally, the opposite enantiomer of any chiral/optically active entity etc.) by using the opposite enantiomer of each chiral and/or optically active substance(s) employed in the appropriate 'original' Example given above, as those skilled in the art understand, and by acting otherwise in a manner exactly similar to that given in the appropriate Example above. So the 'opposite enantiomer' or 'mirror image' of each product described in the above Examples is obtained.

Example 31

Cell lines and tumor-bearing mice. Production of tumors and metastases.

"ODC sarcoma cells", called herein also "OS cells", were employed in some experiments and were originally derived from tumors that were formed in nude mice to which had been administered NIH3T3 mouse fibroblasts transformed by virtue of ornithine decarboxylase (ODC) overexpression and have been described earlier (Auvinen et al., 1992; Auvinen et al., 1997).

A Kaposi's sarcoma cell line, KS1767, called herein "KS", was also employed in some experiments. Also this cell line has been described previously (Herndier et al., 1996). The human melanoma cells line C8161 (called herein below simply "melanoma") was also used and has been described by Welch et al. (1991).

The cell lines were cultured in Dulbecco's Modified Eagle's Medium (DMEM; Bio-Whittaker) supplemented with 5-10 % fetal calf serum (FCS; Bio-Whittaker), 1 % L-glutamine (Bio-Whittaker) and 1% penicillin/streptomycin (Bio-Whittaker).

For production of experimental tumors, the OS, KS or melanoma cells mentioned above (0.5×10^6 cells) were injected subcutaneously into both flanks of nude mice of the strains Balb/c Ola Hsd-nude or NMRI/nu/nu (all mice of both strains were from Harlan Laboratories). Tumors were harvested when they had reached a weight of about 0.4 g.

Metastases (mostly formed in the lungs) were produced by injection of OS or melanoma cells i.v. into Balb/c Ola Hsd-nude mice. The mice were kept 4-6 weeks, and then targeting experiments were performed.

Example 32

General procedures for preparation of glutathione-S-transferase (GST) -fusion proteins. Preparation of fusion proteins for use as targeting agents/units.

Synthetic DNA sequences encoding the desired amino acid sequences were produced by annealing two complementary oligonucleotides (Genset SA) comprising either EcoRI or BamHI restriction sites in their 5' ends, and a stop codon in the 3' end of the coding strand, at 65 °C for 1 min. For production of the DNA encoding the targeting peptides, partially overlapping oligonucleotides were used and the double-stranded product was synthesized at 72 °C for 30 s in the presence of free dNTPs.

The following oligonucleotides were used for production of the DNA encoding the different targeting sequences:

GCIREC: forward primer: 5' -CGGGATCCGGGTGTATTCGGGAGTGTTGA- 3'; reverse primer: 5' -GGAATTCTCAACACTCCCGAATACACCC- 3'

IQLRDWGFIL: forward primer:
5' -CGGGATCCATTCAGTTGCGTGATTGGGGTTTTATTTTGTGAGAATTCC- 3'
reverse primer: 5'
-GGAATTCTCACAAAATAAAACCCCAATCACGCAACTGAATGGATCCCG- 3'

IQLRD: forward primer: 5′-CGGGATCCATTCAGTTGCGTGATTGAGAATTCC- 3′; reverse primer: 5′-GGAATTCTCAATCACGCAACTGAATGGATCCCG- 3′

LRELSMGYFK: forward primer:
5' -CGGGATCCTTGCGTGAGTTGAGTATGGGTTATTTTAAGTGAGAATTCC- 3'
reverse primer:

5' -GGAATTCTCACTTAAAATAACCCATACTCAACTCACGCAAGGATCCCG- 3'

LRELS: forward primer: 5' –CGGGATCCTTGCGTGAGTTGAGTTGAGAATTCC- 3'
reverse primer: 5' –GGAATTCTCAACTCAACTCACGCAAGGATCCCG- 3'

CERIC: forward primer: 5' –CGGGATCCTGTGAGCGGATTTGTTGAGAATTCC- 3'
reverse primer: 5' -GGAATTCTCAACAAATCCGCTCACAGGATCCCG- 3'

GIRE: forward primer: 5′ -CGGGATCCGGTGAGCGGATTTGAGAATTC- 3′, reverse primer 5′-GGAATTCTCAAATCCGCTCACCGGATCCC- 3′

IRE: forward primer: 5′ -CGGGATCCATTCGGGAGTGAGAATTC- 3′, reverse primer: 5' –GGAATTCTCACTCCCGAATGGATCCC- 3′

GERI: forward primer: 5′ -CGGGATCCGGTGAGCGGATTTGAGAATTC- 3′, reverse primer: 5' –GGAATTCTCAAATCCGCTCACCGGATCCC- 3′

ERI: forward primer: 5′ -CGGGATCCGAGCGGATTTGAGAATTC- 3′, reverse primer: 5' –GGAATTCTCAAATCCGCTCGGATCCC- 3′

The double-stranded products were digested with BamHI and EcoRI and the fragments were ligated into the corresponding restriction sites of the pGEX-2TK vector (AmershamPharmacia Biotech). Competent *E. coli* BL21 bacteria were transformed with the ligation mixture and transformants were screened using colony-PCR (PCR = polymerase chain reaction). Primers specific for the insert-flanking regions of the pGEX vector were used for identification of the inserts (forward primer: 5'-GCATGGCCTTTGCAGGG-3'; reverse primer: 5'-AGCTGCATGTGTCAGAGG-3'). DNA was isolated from positive clones using a QIAprep Spin miniprep kit (cat. no. 27106; Qiagen).

The DNA sequence of the constructs was determined with an ALF automated DNA sequencer (AmershamPharmacia Biotech) using the same primers as for the colony-PCR. Large scale production and purification of GST and of GST-fusion proteins was done according to AmershamPharmacia's instructions (GST detection module instructions, Technical document XY0460012-Rev.8.pdf; Uppsala, Sweden). The size, quantity and purity of the GST-fusion proteins were examined by SDS-PAGE (= sodium-dodecyl-sulphate polyacrylamide-gel electrophoresis).

Example 33

General procedure for detection/analysis/visualization of tumor targeting in tumor-bearing mice. Immunohistochemistry. Some practical uses/applications of some targeting agents.

The nude mice described above were employed. Tumor-bearing or metastase-bearing mice were anesthesized by administering 0.02 ml/g body weight Avertin [10 g 2,2,2-tribromoethanol (Fluka) in 10 ml 2-methyl-2-butanol (Sigma Aldrich)] intraperitoneally (i.p.).

For localization of targeting peptide(s)/peptidomimetic analogues(s)/peptidyl analogue(s)/agent(s)/unit(s), KS, OS or melanoma tumor-bearing or metastase-bearing NMRI nude mice were anesthesized and 1 or 2 mg of GST-fusion protein (comprising targeting peptide/peptidomimetic analogue/peptidyl analogue/unit) in DMEM, or GST alone in DMEM as control, was injected intravenously (i.v.) or i.p.. Alternatively, either 1 or 2 mg of biotinylated synthetic peptide/peptidomimetic analogue/peptidyl analogue/agent/unit was injected i.v. 5-10 min after the i.v. injections, the mice were perfused via the heart using a winged infusion 25G needle set (Terumo) with 50 ml DMEM. Then, their organs were dissected and frozen in liquid nitrogen. In some cases, a GST-fusion protein was injected i.v. as above, and then the mice were sacrified after 30 min, 4 h, 8 h or 18 h, without perfusion, and then tumors and control organs were dissected and frozen in liquid nitrogen. Intraperitoneally injected mice were kept 24 h before sacrification, and then tumors and control organs were dissected and frozen as above.

The GST-fusion proteins (and GST as control) were detected on 10 micrometer cryosections by goat anti-GST antiserum (AmershamPharmacia).

Biotinylated peptides/peptidomimetic analogues/peptidyl analogues (targeting agents) were detected on 10 micrometer cryosections using AB (avidin-biotin) -complex containing avidin, and biotinylated HRP (Vectastain ABC-kit, cat no. PK6100; Vector Laboratories) with diaminobenzidine (DAB substrate kit, cat no. 4100, Vector Laboratories).

Examples 34-58

Targeting to various primary tumors and to metastases *in vivo*. Use of targeting motifs and units and agents *in vivo*. Diagnostic use. Histological, immunohistological and histochemical use and use as reagent and for research purposes. Use for detection and related purposes.

Individual targeting Examples are given [for all of the three types of primary tumors (OS, KS, melanoma) described above in Example 31 and for metastases produced as described in said Example] in the specific Examples 34-58 below, the experiments described being

performed employing the general procedures of Example 33. In said specific Examples, it is shown that the appropriate targeting motifs and units, and agents comprising them, target specifically to primary tumors and to metastases *in vivo* but not to normal tissue(s)/organ(s). Thus, they can be used for targeting purposes [including targeting for diagnosis, therapy, detection, research etc. purpose(s)] *in vivo*.

Example 34

The GST-GCIREC fusion protein (Example 32) was studied (according to the general procedures of Example 33) in a mouse bearing an OS tumor in its flank. 1 mg of the fusion protein was injected i.v. and was allowed to circulate in the animal for 30 min. The fusion protein was shown to target specifically to the OS tumor *in vivo*.

Example 35

The GST-GCIREC fusion protein (Example 32) was studied (according to the general procedures of Example 33) in a mouse bearing an OS tumor in its flank. 1 mg of the fusion protein was injected i.v. and was allowed to circulate in the animal for 4h. The fusion protein was shown to target specifically to the OS tumor *in vivo*.

Example 36

The GST-GCIREC fusion protein (Example 32) was studied (according to the general procedures of Example 33) in two mice bearing KS tumors in both flanks (2 tumors/mouse). 1 mg of the fusion protein was injected to each mouse, and the animals were perfused after 5-10 min. The fusion protein was shown to target specifically to the KS tumors *in vivo*.

Example 37

The GST-GCIREC fusion protein (Example 32) was studied (according to the general procedures of Example 33) in a mouse bearing a melanoma C8161 tumor in its flank. 1 mg of the fusion protein was injected i.v. and was allowed to circulate in the animal for 30 min. The fusion protein was shown to target specifically to the melanoma tumor *in vivo*.

Example 38

The GST-GCIREC fusion protein (Example 32) was studied (according to the general procedures of Example 33) in a mouse bearing a melanoma C8161 tumor in its flank. 1 mg of the fusion protein was injected i.v. and was allowed to circulate 4 h. The fusion protein was shown to target specifically to the melanoma tumor *in vivo*.

Example 39

The GST-GCIREC fusion protein (Example 32) was studied (according to the general procedures of Example 33) in a mouse bearing OS metastases in the diaphragm and peritoneum. 1 mg of the fusion protein was injected i.v. and the animal was perfused after 5-10 min. The fusion protein was shown to target specifically to these metastases *in vivo*.

Example 40

The GST-GCIREC fusion protein (Example 32) was studied (according to the general procedures of Example 33) in a mouse bearing melanoma C8161 metastases in the lungs. 2 mg of the fusion protein were injected i.v. and were allowed to circulate for 18 h. The fusion protein was shown to target specifically to these metastases *in vivo*.

Example 41

The GST-GCIREC fusion protein (Example 32) was studied (according to the general procedures of Example 33) in a mouse bearing melanoma C8161 metastases in the lungs. 2 mg of the fusion protein were injected i.v. and were allowed to circulate for 8 h. The fusion protein was shown to target specifically to these metastases *in vivo*.

Example 42

The GST-LRELSMGYFK fusion protein (Example 32) was studied (according to the general procedures of Example 33) in a mouse bearing an OS tumor in its flank. 1 mg of the fusion protein was injected i.v. and the animal was perfused after 5-10 min. The fusion protein was shown to target specifically to the OS tumor *in vivo*.

Example 43

The GST-LRELSMGYFK fusion protein (Example 32) was studied (according to the general procedures of Example 33) in a mouse bearing a melanoma C8161 tumor in its flank. 1 mg of the fusion protein was injected i.v. and the animal was perfused after 5-10 min. The fusion protein was shown to target specifically to this tumor *in vivo*.

Example 44

The GST-IQLRDWGFIL fusion protein (Example 32) was studied (according to the general procedures of Example 33) in a mouse bearing a melanoma C8161 tumor in its flank. 1 mg of the fusion protein was injected i.v. and the animal was perfused after 5-10 min. The fusion protein was shown to target specifically to this tumor *in vivo*.

Example 45

The GST-LRELS fusion protein (Example 32) was studied (according to the general procedures of Example 33) in two mice bearing an OS tumor in their flanks. 1 mg of the fusion protein was injected i.v. and the animal was perfused after 5-10 min. The fusion protein was shown to target specifically to the OS tumor *in vivo*.

Example 46

The GST-CERIC fusion protein (Example 32) was studied (according to the general procedures of Example 33) in two mice bearing an OS tumor in their flanks. 1 mg of the fusion protein was injected i.v. and the animal was perfused after 5-10 min. The fusion protein was shown to target specifically to the OS tumor *in vivo*.

Example 47

The GST-CERIC fusion protein (Example 32) was studied (according to the general procedures of Example 33) in two mice bearing a melanoma C8161 tumor in their flanks. 1 mg fusion protein was injected i.v. and the animals were perfused after 5-10 min. The fusion protein was shown to target specifically to the melanoma tumor *in vivo*.

Example 48

The GST-GCIREC fusion protein (Example 32) was studied (according to the general procedures of Example 33) in four mice bearing a KS tumor in their flanks. 2 mg fusion protein were injected i.p. and the protein was allowed to circulate 24 h. The fusion protein was shown to target specifically to this tumor *in vivo*.

Example 49.

The targeting agent Bio_4-K_2-K-AhxCIRECG (cyclic by virtue of cystine) was prepared as described in Example 29 above and was studied (according to the general procedures of Example 33) in a mouse bearing an OS tumor in its flank. 1 mg of this targeting agent (four-fold biotinylated peptide) was injected i.v.. The agent was then allowed to circulate for 30 min and was shown to target specifically to this tumor *in vivo*.

Example 50

The targeting agent Bio_4-K_2-K-AhxCIRECG (cyclic by virtue of cystine) was prepared as described in Example 29 above and was studied (according to the general procedures of Example 33) in a mouse bearing a C8161 melanoma tumor in its flank. 1 mg of this

targeting agent (four-fold biotinylated peptide) was injected i.v.. The agent was then allowed to circulate for 30 min and was shown to target specifically to this tumor *in vivo*.

Example 51

The targeting agent Bio_4-K_2-K-AhxCIRECG (cyclic by virtue of cystine) was prepared as described in Example 29 above and was studied (according to the general procedures of Example 33) in a mouse bearing a C8161 melanoma tumor in its flank. 2 mg of this targeting agent (four-fold biotinylated peptide) were injected i.v.. The agent was then allowed to circulate for 30 min and was shown to target specifically to this tumor *in vivo*.

Example 52

The targeting agent Bio_4-K_2-K-AhxCIRECG (cyclic by virtue of cystine) was prepared as described in Example 29 above and was studied (according to the general procedures of Example 33) in a mouse bearing an OS tumor in its flank. 2 mg of this targeting agent (four-fold biotinylated peptide) were injected i.v.. The agent was then allowed to circulate for 30 min and was shown to target specifically to this tumor *in vivo*.

Example 53

The targeting agent Bio-DIREK (prepared as described in Example 23 above; *i.e.*, the biotinylated cyclic peptide DIREK, comprising one biotin moiety) was studied (according to the general procedures of Example 33) in a mouse bearing a C8161 melanoma tumor in its flank. 1 mg of the targeting agent (biotinylated peptide) was injected i.v., the animal was perfused after 10 min and the agent was shown to target specifically to this tumor *in vivo*.

Example 54

The targeting agent Bio-DIREK (prepared as described in Example 23 above; *i.e.*, the biotinylated cyclic peptide DIREK, comprising one biotin moiety) was studied (according to the general procedures of Example 33) in a mouse bearing an OS tumor in its flank. 1 mg of the targeting agent (biotinylated peptide) was injected i.v., the animal was perfused after 10 min and the agent was shown to target specifically to this tumor *in vivo*.

Example 55

The targeting agent Bio-DIREK (prepared as described in Example 23 above; *i.e.*, the biotinylated cyclic peptide DIREK, comprising one biotin moiety) was studied (according to the general procedures of Example 33) in a mouse bearing a C8161 melanoma tumor in its flank. 2 mg of the targeting agent (biotinylated peptide) were injected i.v., the animal

was perfused after 10 min and the agent was shown to target specifically to this tumor *in vivo*.

Example 56

The targeting agent Bio-DIREK (prepared as described in Example 23 above; *i.e.*, the biotinylated cyclic peptide DIREK, comprising one biotin moiety) was studied (according to the general procedures of Example 33) in a mouse bearing an OS tumor in its flank. 2 mg of the targeting agent (biotinylated peptide) were injected i.v., the animal was perfused after 10 min and the agent was shown to target specifically to this tumor *in vivo*.

Example 57

The targeting agent (biotinylated cyclic peptide) Bio-CIRECG, made according to Example 15 above) was studied (according to the general procedures of Example 33) in a mouse bearing a melanoma C8161 tumor in its flank. 1 mg of the targeting agent was injected i.v. and the targeting agent was allowed to circulate for 30 min, and was shown to target specifically to the melanoma tumor *in vivo*.

Example 58

The targeting agent (biotinylated cyclic peptide) Bio-CIRECG, made according to Example 15 above) was studied (according to the general procedures of Example 33) in a mouse bearing an OS tumor in its flank. 1 mg of the targeting agent was injected i.v. and the targeting agent was allowed to circulate for 30 min, and was shown to target specifically to this tumor *in vivo*.

REFERENCES

Adams, GP, Schier R. Generating improved single-chain Fv molecules for tumor targeting. J Immunol Methods 1999;231:249-60.

Arap, W., Pasqualini, R., and Ruoslahti, E. (1998). Chemotherapy targeted to tumor vasculature. Curr. Op. Oncol. 10: 560-565.

Auvinen, M, Paasinen, A., Andersson, L. C., and Hölttä, E.(1992). Ornithine decarboxylase activity is critical for cell transformation. Nature (Lond.), 360: 355-58.

Auvinen, M, Laine, A., Paasinen-Sohns, A., Kangas, A., Saksela, O., Andersson, L. C., and Hölttä, E. (1997). Human ornithine decarboxylase-overproducing NIH3T3 cells induce rapidly growing, highly vascularized tumors in nude mice. Cancer Res. 57: 3016-25.

Bachem AG, SASRIN ™ , A review of its manyfold applications including many useful procedures, comlied by Mergler M., 2nd revised and enlarged edition 1999, 1999 by BACHEM AG, CH-4416 Bubendorf, Switzerland.

Bachem 2001, Peptides and Biochemicals, Immunochemicals, The New 2001 BACHEM catalog, BACHEM AG, Hauptstrasse 144, CH-4416 Bubendorf – Switzerland.

Beckstead, J. H., Wood, G. S., and Fletcher V. (1985). Evidence for the origin of Kaposi's sarcoma from lymphatic endothelium. Am. J. Pathol. 119: 294-300.

Biosystems Solutions, Issue 2 – September 2001, p. 30. AB Applied Biosystems.

Brown, J. M., and Giaccia, A. J. (1998). The unique physiology of solid tumors: opportunities (and problems) for cancer therapy. Cancer Res. 58: 1408-1416.

Chan, W.C. Bycroft, B.W., Evans, D.J. and White, P.D. A novel 4-aminobenzyl ester-based carboxy-protecting group for synthesis of atypical peptides by Fmoc-Bu^t solid-phase chemistry. (1995) J. Chem. Soc., Chem. Commun., 1995, p. 2209.

Curnis, F., Sacchi, A., Borgna, L., Magni, F., Gasparri, A., and Corti, A. (2000). Enhancement of tumor necrosis factor alpha antitumor immunotherapeutic properties by targeted delivery to aminopeptidase N (CD13). Nat. Biotechnol. 11: 1185-1190.

Elo, H. (1987) Unusual Organ Distribution of Chelated Copper in Rats, Naturwissenschaften 74, S 245.

Elo, H. (1987). Reaction of the Antiproliferative and Antineoplastic Agent *trans*-Bis(salicylaldoximato)copper(II) and Related Chelates with Glutathione and Cysteine. Correlation between Reactivity and Biological Activity. Inorganica Chimica Acta, 136 (1987) L33-L35.

Elo, H. and Lumme, P. (1986). Antiproliferative Activity of Derivatives of *trans*-Bis(salicylaldoximato)copper(II) *in vitro*. Some in vivo Properties of the Parent Compound. Z. Naturforsch. 41c, 951-955.

Elo, H. and Lumme, P. (1986). *trans*-Bis(salicylaldoximato)copper(II) and its derivatives as antiproleferative and antineoplastic agents: a review. Inorganica Chimica Acta, 136 (1987) 149-153.

Ellerby, H. M., Arap, W., Ellerby, L. M., Kain, R., Andrusiak, R., Rio, G. D., Krajewski, S., Lombardo, C. R., Rao, R., Ruoslahti, E., Bredesen, D. E., and Pasqualini, R. 1(1999). Anti-cancer activity of targeted pro-apoptotic peptides. Nat. Med. 9: 1032-1038.

Fluka Chemika, Peptide and Peptidomimetic Synthesis, Reagents for Drug Discovery, 2000 Fluka Chemie GmbH, Buchs, Fluka, Speciality Chemicals and Analytical Reagents.

Folkman, J. (1997). Addressing tumor blood vessels. Nat. Biotechnol. 15: 510.

Folkman, J. (1999). Angiogenic zip code. Nat. Biotechnol. 17: 749

Herndier BG, Werner A, Arnstein P, Abbey NW, Demartis F, Cohen RL, Shuman MA, Levy JA. (1994). Characterization of a human Kaposi's sarcoma cell line that induces angiogenic tumors in animals. AIDS 8:575-81.

Hidalgo, M., and Eckhardt, S. G. (2001). Development of matrix metalloproteinases inhibitors in cancer therapy. J. Natl. Cancer Inst. 93: 178-193.

Hirschmann, R., Yao, W., Arison, B., Maechler, L., Rosegay, A., Spengeler, P.A., and Smith, A.B. (1998), Synthesis of the first tricyclic homodetic peptide. Use of Coordinated Orthogonal Deprotection to Achieve Directed Ring Closure. Tetrahedron 54 (1998) 7179-7202.

Hong F. D., and Clayman, G. L. (2000). Isolation of a peptide for targeted drug delivery into human head and neck solid tumors. Cancer Res. 60: 6551-6556.

Houghten, R.A., Pinilla C., Appel J.R., Blondelle S.E., Dooley C.T., Eichler J., Nefzi A., Ostresh J.M. Mixture-based synthetic combinatorial libraries. J. Med. Chem. 1999;42:3743-78.

Izbicki, J. R., Hosch, S. B., Pichlmeier, U. wt al. (1997). Prognostic value of immunohistochemically identifiable tumor cells in lymph nodes of patients with completely resected esophageal cancer. N. Engl. J. Med. 23: 1188-1194.

Jain, R. K. (2001). Normalizing tumor vasculature with anti-angiogenic therapy: A new paradigm for combination therapy. Nat. Med. 7: 987-989.

Jankowski, J. A., Wright, N. A., Meltzer, S. J. et al., (1999). Molecular evolution of the metaplasia-dysplasia-adenocarcinoma sequence in the esophagus. Am. J. Pathol. 154: 965-973.

Kaipainen, A., Korhonen, J., Pajusola, K., Aprelikova, O., Persico, M. G., Terman, B. I., and Alitalo, K. (1993). The related FLT4, FLT1 and KDR receptor tyrosine kinases show distinct expression patterns in human fetal endothelial cells. J. Exp. Med. 178: 2077-88.

Kaipainen, A., Korhonen, J., Mustonen, T., van Hindsberg, V. W. M., Fong, G.-H., Dumont, D., Breitman, M., and Alitalo, K. (1995). Expression of the FLT4 receptor tyrosine kinase becomes restricted to lymphatic endothelium during development. Proc. Natl. Acad. Sci. USA 92: 3566-70.

Kerbel, R. S. (2000). Tumor angiogenesis: past present and the near future. Carcinogenesis 21: 505-515.

Kjeldsen, L., Johnsen, A. H., Sengelov, H., and Borregaard, N. (1993). Isolation and primary structure of NGAL, a novel protein associated with human neutrophil gelatinase. J. Biol. Chem. 268: 10425-10432.

Koivunen, E., Arap, W., Valtanen, H., Rainisalo, A., Penate Medina, O., Heikkilä, P., Kantor, C., Gahmberg, C.G., Salo, T., Konttinen, Y.T., Sorsa, T., Ruoslahti, E. and Pasqualini, R. (1999). Tumor targeting with a selective gelatinase inhibitor. Nat. Biotechnol. 17: 768-773.

Koivunen, E., Wang, B., Dickinson, C.D. and Ruoslahti, E. (1994). Peptides in cell adhesion research. Meth. Enzymol. 245: 346-369.

Mergler, M. and Durieux, J.P., BACHEM AG, 2000 by BACHEM AG, CH-4416 Bubendorf, Switzerland.

Naknishi, H, and Kahn, M. (1996). Design of peptidomimetics. *In*: The practice of medical chemistry, pp. 571-590. Academic Press

Nargund, R.P., Patchett, A.A., Bach, M.A. Murphy, M.G., Smith, R.G. (1998) Peptidomimetic growth hormone secretagogues. Design considerations and therapeutic potential. J.Med. Chem. 1998; 41:3103-27.

Neri, D., Carnemolla, B., Nissim, A., Leprini, A. Querze, G., Balza, E., Pini, A, Tarli, L, Halin, C., Neri, P., Zardi, L, and Winter, G. (1997). Targeting by affinity-matured recombinant antibody fragments of an angiogenesis associated fibronectin isoform. Nat. Biotechnol. 12:1271-5.

Nicklin, S. A., White, S. J., Watkins, S. J., Hawkins, R. E., Baker, A. H. (2000). Selective targeting of gene transfer to vascular endothelial cells by use of peptides isolated by phage display. Circulation 102: 231-237.

Novabiochem # 1 for innovation. Novabiochem 2000 Catalog, Calbiochem-Novabiochem AG, Weidenmattweg 4 Läufelfingen, Switzerland, 2000.

Ohkubo, S., Miyadera, K., Sugimoto, Y., Matsuo, K., Wierzba, K., and Yamada, Y. (1999). Identification of subsrtate sequences for membrane type-1 matrix metalloproteinases using bacteriophage peptide phage display library. Biochem. Biophys. Res. Comm. 266: 308-313.

Pasqualini, R., Koivunen, E., and Ruoslahti, E. (1997). α_v integrins as receptors for tumor targeting by circulating ligands. Nature Biotech. 15: 542-546.

Popkov, M., Lussier, I., Medvedkine, V., Estève, P-O., Alakhov, V. and Mandeville, R.(1998). Multidrug-resistance drug-binding peptides generated by using a phage display library. Eur. J. Biochem. 251: 155-163.

Prochiantz, A. (1996). Getting hydrophilic compounds into cells: lessons from homeopeptides. Curr. Op. Neurobiol. 6: 629-634.

Prochiantz, A. (1999). Homeodomain-derived peptides. In and out of the cells. Ann. New York Acad. Sci. 886: 172-179

Promega Notes Magazine, Promega Corporation, Number 74, InCELLect™ Cell-Permeable Peptides, 2000.

Protective Groups in Organic Synthesis, Third Edition, Theodora W. Greene, Peter G.M. Wuts, 1999, John Wiley & Sons, Inc. ISBN: 0-471-16019-9

Pulli, T., Koivunen, E., and Hyypiä, T. (1997). Cell-surface interactions of Echovirus 22. J. Biol. Chem. 272: 21176-21180.

Smith G. P., and Scott, J. K. (1993). Libraries of peptides and proteins displayed on filamentous phage. Met. Enzymol. 217: 228-257.

The BACHEM Practise of SPPS, (2000) Tips and tricks from the experts at BACHEM, compiled by Mergler, M. and Durieux, J.P., BACHEM AG, 2000 by BACHEM AG, CH-4416 Bubendorf, Switzerland.

The Combinatorial Chemistry Catalog & Solid Phase Organic Chemistry (SPOC) Handbook, Novabiochem # 1 for innovation, Switzerland, Calbiochem-Novebiochem AG Weidenmattweg 4, CH-4448 Läufellingen, Switzerland, 1998-1999.

Turk, B. E., Huang, L. L., Piro, E. T., Cantley, L. C. (2001). Determination of protease cleavage site motifs using mixture-based oriented peptide libraries. Nat. Biotechnol. 19: 661-667.

Welch, D. R., Bisi, J. E., Miller, B. E., Conaway, D., Seftor, E. A., Yohem, K. H. et al. (1991). Characterization of a highly invasive and spontaneously metastatic human malignant melanoma cell line. Int. J. Cancer 47: 227-237.

Yue, C., Thierry, J. and Potier, P. (1993) 2-phenyl isopropyl esters as carboxyl terminus protecting groups in the fast synthesis of peptide fragments, Tetrahedron Letters 34(2): 323-326.

Claims:

1. A targeting agent comprising

- one or more targeting unit(s), and
- one or more effector unit(s),

characterized in that the targeting unit comprises one or more motif(s)

Dd-Ee-Ff

and/or one or more salt(s), ester(s), amide(s), hydrazide(s), *N*-substituted amide(s), *N*-substituted hydrazide(s), hydroxamic acid -type derivative(s), *C*-terminally decarboxylated analogue(s), *N*-substituted derivative(s), and/or any related analogue(s) and/or derivative(s), and/or their combination(s), of one or more such motif(s),

wherein

Dd is either Aa or Bb or Cc or Aa′ or Bb′ or Cc′, and
Ee is either Aa or Bb or Cc or Aa′ or Bb′ or Cc′, and
Ff is either Aa or Bb or Cc or Aa′ or Bb′ or Cc′, and
Dd-Ee-Ff comprises Aa/Aa′and Bb/Bb′ and Cc/Cc′, and

wherein

Aa is the L- or D- form of isoleucine, leucine, *tert*-leucine or valine, or a structural and/or functional analogue thereof comprising in its side chain a branched, non-branched and/or alicyclic structure with at least two similar or different atoms selected from the group of carbon atoms, silicon atoms, halogen atoms bonded to one or more carbon(s), ether-oxygens and thioether-sulphurs;

Bb is the L- or D- form of arginine, homoarginine or canavanine, or a structural and/or functional analogue thereof comprising at least one guanyl and/or amidino group or a related group that has or can through protonation obtain a delocalized positive charge;

Cc is the L- or D- form of glutamic acid or aspartic acid, or a structural and/or functional analogue thereof, comprising in its side chain at least one carboxyl group or esterified carboxyl group;

Aa′ is a branched or non-branched or cyclic non-aromatic, lipophilic and/or hydrophobic amino acid or amino acid analogue or derivative or a structural and/or functional analogue thereof, or an amino acid or carboxylic acid or amino acid analogue or derivative or carboxylic acid analogue or derivative that has one or more lipophilic carborane-type and/or other lipophilic boron-containing side chain(s) or its/their equivalent(s) or another lipophilic cage-type structure;

Bb′ is an amino acid or amino acid analogue or derivative or a structural and/or functional analogue thereof, that comprises one or more guanyl group(s) and/or amidino group(s) and/or its/their analogue(s) and/or derivative(s) and/or structural and/or functional equivalent(s) and/or one or more group(s) that comprise(s) at least two nitrogen atoms each and has/have or can gain a delocalized positive charge;

Cc′ is an amino acid or amino acid analogue or derivative or a structural and/or functional analogue thereof that comprises: one or more side-chain carboxyl group(s) and/or esterified carboxyl group(s), and/or ketoxime and/or aldoxime and/or hydroxamic acid group(s) and/or ketone- and/or aldehyde-carbonyl(s),

and/or the motif(s) Dd-Ee-Ff or one or more of them is/are structural and/or functional analogue(s) of a structure or structures where Dd-Ee-Ff is as defined above;

and/or the targeting agent comprises one or more of the following:

- any salt(s)
- any ester(s)
- any amide(s)
- any hydrazide(s)
- any *N*-substituted amide(s)
- any *N*-substituted hydrazide(s)
- any hydroxamic acid derivative(s)
- any decarboxylated analogue(s)
- any *N*-substituted derivative(s)
- any other related derivative(s)
- any other related analogue(s)
- any combination of any of such salt, derivative and/or analogue types,

of the targeting agent as defined above.

2. The targeting agent according to claim 1, c h a r a c t e r i z e d in that said targeting unit(s) and/or one or more of them exhibit(s) selective binding to one or more type(s) of: tumors and/or cancer(s) and/or tumor cells and/or cancer cells and/or malignant cells and/or transformed cells and/or tumor tissues and/or cancer tissues and/or malignant tissues and/or transformed tissues and/or leukemia cells and/or malignant blood cells and/or tranformed blood cells and/or related cells and/or tissues and/or tumor endothelium and/or activated endothelium and/or angiogenic endothelium and/or tumor-endothelium cells and/or activated-endothelium cells and/or angiogenic endothelium cells, and/or their like.

3. The targeting agent according to claim 1 or claim 2, c h a r a c t e r i z e d in that said targeting unit(s) and/or one or more of them exhibit(s) selective binding to one or more type(s) of: tumors and/or cancer(s) and/or tumor cells and/or cancer cells and/or malignant cells and/or transformed cells and/or tumor tissues and/or cancer tissues and/or malignant tissues and/or transformed tissues and/or leukemia cells and/or malignant blood cells and/or tranformed blood cells and/or related cells and/or tissues and/or tumor endothelium and/or activated endothelium and/or angiogenic endothelium and/or tumor-endothelium cells and/or activated-endothelium cells and/or angiogenic endothelium cells, and/or their like, *in vivo* and/or *in vitro* and/or *ex vivo* and/or *in situ*.

4. The targeting agent according to any one of the previous claims, c h a r a c t e r i z e d in that said targeting unit(s) and/or one or more of them exhibit(s) selective binding to one or more type(s) of: tumors and/or cancer(s) and/or tumor cells and/or cancer cells and/or malignant cells and/or transformed cells and/or tumor tissues and/or cancer tissues and/or malignant tissues and/or transformed tissues and/or leukemia cells and/or malignant blood cells and/or tranformed blood cells and/or related cells and/or tissues and/or tumor endothelium and/or activated endothelium and/or angiogenic endothelium and/or tumor-endothelium cells and/or activated endothelium cells and/or angiogenic endothelium cells, and/or their like, *in vivo*.

5. The targeting agent according to any one of the previous claims, c h a r a c t e r i z e d in that said targeting unit(s) and/or one or more of them exhibit(s) selective binding to one or more type(s) of: tumors and/or cancer(s) and/or tumor cells and/or cancer cells and/or malignant cells and/or transformed cells and/or tumor tissues and/or cancer tissues and/or malignant tissues and/or transformed tissues and/or leukemia cells and/or malignant blood cells and/or tranformed blood cells and/or related cells and/or tissues and/or tumor endothelium and/or activated endothelium and/or angiogenic endothelium and/or tumor-endothelium cells and/or activated-endothelium cells and/or angiogenic endothelium cells, and/or their like, *in vitro* and/or *ex vivo*.

6. The targeting agent according to any one of the previous claims, wherein the targeting unit(s) or one or more of them is/are capable of binding to one or more type(s) of: primary tumors and/or cancers, and/or tumor/cancer endothelium, and/or tumor/cancer metastases, and/or residive/residual tumors and/or cancers, and/or recurred/recurrent/relapsed tumors and/or cancers, and/or tumor cells; *in vivo* and/or *in vitro* and/or *ex vivo* and/or *in situ*.

7. The targeting agent according to any one of the previous claims, wherein the targeting unit(s) and/or one or more of them and/or the motif(s) Dd-Ee-Ff and/or one or more of them

is/are cyclic and/or form(s) part(s) of one or more cyclic structure(s); and/or

is/are not cyclic and do(es) not form part(s) of a cyclic structure or cyclic structures, and/or is/are linear; and/or

is/are cyclic and/or form(s) part(s) of one or more cyclic structure(s) in such a way that the motif(s) and/or one or more of them is/are wholly included in one or more cyclic structure(s); and/or

is/are branched and/or is/are not branched and/or is/are branched and cyclic.

8. The targeting agent according to any one of the previous claims, wherein

the amount and/or location(s) of cyclic structure(s) may vary and/or change, and/or be in a state of equilibrium and/or fluctuation and/or related phenomenon/phenomena, and/or be uncertain and/or indifferent and/or undetermined, and/or wherein the degree of cyclicity at any potentially cyclic location may be partial and/or may be essentially total and/or may be essentially none and/or may be variant;

and/or wherein

the targeting unit(s) or one or more of them may and/or may not be cyclic, and/or the amount and/or location(s) of cyclic structure(s) may vary and/or change.

9. The targeting agent according to any one of the previous claims, wherein the total number of amino acid and/or amino acid analogue residues in the targeting unit or in each one of the targeting units is no more than 11, preferably no more than 9, still more preferably no more than 8, still more preferably no more than 7, and most preferably no more than 5.

10. The targeting agent according to any one of the previous claims, wherein the motif(s) Dd-Ee-Ff is/are selected from the group of

Aa/Aa′- Bb/Bb′- Cc/Cc′,
Aa/Aa′- Cc/Cc′- Bb/Bb′,
Bb/Bb′- Aa/Aa′- Cc/Cc′,
Bb/Bb′- Cc/Cc′- Aa/Aa′,
Cc/Cc′- Aa/Aa′- Bb/Bb′ and
Cc/Cc′- Bb/Bb′- Aa/Aa′,

preferably from the group of

Aa/Aa′- Bb/Bb′- Cc/Cc′ and
Cc/Cc′- Bb/Bb′- Aa/Aa′.

11. The targeting agent according to any one of the previous claims, wherein the motif(s) Dd-Ee-Ff or one or more of them is/are

Aa/Aa′- Bb/Bb′- Cc/Cc′.

12. The targeting agent according to any one of the previous claims, wherein the motif(s) Dd-Ee-Ff or one or more of them is/are selected from the group of

Aa-Bb-Cc,
Aa-Cc-Bb,
Bb-Aa-Cc,
Bb-Cc-Aa,
Cc-Aa-Bb and
Cc-Bb-Aa,

preferably from the group of

Aa-Bb-Cc and
Cc-Bb-Aa.

13. The targeting agent according to any one of the previous claims, wherein the motif(s) Dd-Ee-Ff or one or more of them is/are

Aa-Bb-Cc.

14. The targeting agent according to any one of the previous claims, wherein the cyclic structure(s) or one or more of them

is/are formed through one or more peptide bond(s) and/or other amide bond(s) and/or disulphide bond(s) and/or ester bonds, in addition to bonds that exist inside the motif(s) Dd-Ee-Ff, and/or

comprise(s) at least one lactone and/or lactam bond, and/or

comprise(s) at least one disulphide bond, and/or

is/are formed through one or more hydrazone and/or one or more hydrazide moiety/moieties and/or comprises one or more C-N-N-C and/or C=N-N=C and/or C-N-N=C and/or C-N=N-C moiety/moieties.

15. The targeting agent according to any one of the previous claims, that comprises two or more identical and/or similar and/or different motifs Dd-Ee-Ff and/or two or more identical and/or similar and/or different targeting units.

16. The targeting agent according to any one of the previous claims, that comprises

two or more identical and/or similar and/or different effector units, and/or

two or more identical and/or similar effector units, and/or

two or more effector units, both or all or some of which are not identical with each other.

17. The targeting agent according to any one of the previous claims, that comprises one or more structure(s)

Kk-Dd-Ee-Ff-Ll

wherein the motif(s) Dd-Ee-Ff is/are as defined in claim 1, and

Kk and Ll, independently of each other, each comprise one or more structural fragment(s)

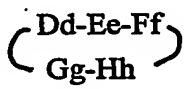
and/or functional group(s) that can be used to form a bond and/or linkage between Kk and Ll so that a cyclic structure is formed, and/or Kk and Ll are parts of a structure so that Kk-Dd-Ee-Ff-Ll is cyclic,

and/or

Kk and Ll, independently of each other, each comprise one or more structural fragment(s) and/or functional group(s) that can be used to form: a lactame structure, or a lactam-type structure, or a lactone structure, or a lactone-type structure, or a cyclic structure comprising a cystine, or a cyclic structure comprising a cystine-type structure, or a cyclic structure comprising another disulphide bridge, or a hydrazone- and/or hydrazide-type bridge or related type of bridge; between Kk and Ll so that a cyclic structure is formed, and/or

Kk and Ll are parts of a lactone and/or a lactone-type structure, and/or a cyclic structure comprising a cystine, and/or a cyclic structure comprising a cystine-type structure, or a cyclic structure comprising another disulphide bridge; so that Kk-Dd-Ee-Ff-Ll is cyclic.

18. The targeting agent according to any one of the previous claims, wherein the cyclic structure(s) or one or more of them is/are and/or comprise(s)



wherein Gg-Hh is/are selected from the group of:

(a) cystine (i.e., Gg and Hh are cysteines that are connected to each other with a disulphide bridge);
(b) two amino acids directly connected to each other via a peptide bond;
(c) two amino acid analogues connected to each other via a peptide bond;
(d) more than two amino acid(s) and/or amino acid analogue(s) connected to each other via one or more peptide bond(s) and/or amide bond(s) and/or one or more disulphide bridge(s);
(e) a cystine-type structure where Hh and Gg independently of each other are either an amino acid or another structure that comprises an 'oxidized thiol' moiety and a disulphide bridge existing between them; and
(f) two structures comprising each maximally 20 non-hydrogen atoms and an unlimited number of hydrogen atoms, either one or both of which are/is not an amino acid, connected to each other with a peptide bond.

19. The targeting agent according to any one of the previous claims, wherein the targeting

unit comprises or each of the targeting units independently comprises 3 to 40 amino acid(s) and/or structural and/or functional analogue(s) of amino acid(s), preferably 3 to 15 amino acid(s) and/or structural and/or functional analogue(s) of amino acid(s), more preferably 3 to 8 amino acid(s) and/or structural and/or functional analogue(s) of amino acid(s).

20. The targeting agent according to any one of the previous claims, wherein

the motif Dd-Ee-Ff or each one of the motifs Dd-Ee-Ff forms part of a structure comprising at least two units of cysteine and/or homocysteine and/or other amino acid(s) and/or amino acid analogue(s) comprising a thiol (-SH) group each that are spaced apart by a number of 3 to 20 intermediary amino acid(s) and/or amino acid analogue(s) and interconnected by a disulphide bond, forming a cyclic structure or cyclic structures in which the motif(s) Dd-Ee-Ff is/are formed by the intermediary amino acid(s) and/or amino acid analogue(s), said cyclic structure(s) being defined by the cysteine unit(s), homocysteine unit(s) and/or other amino acid and/or amino acid analogue unit(s) comprising a thiol (-SH) group each, the intermediary amino acid(s) and/or amino acid analogue(s) and the disulphide bond,

and/or

the motif Dd-Ee-Ff forms or each one of the motifs Dd-Ee-Ff form or one or more of them each form(s) part of a structure comprising, in addition to the motif(s) Dd-Ee-Ff: two units of amino acid(s) and/or amino acid analogue(s) and/or other type(s) of molecule(s) and/or fragment(s) whose individual molecular weight is no more than 270; that are spaced apart by a number of 3 to 20 intermediary amino acid(s) and/or amino acid analogue(s); and interconnected by a lactam bond or a lactam-type bond or a lactone bond or a lactone-type bond or an amide bond or a hydrazone- and/or hydrazide-type bridge, or by being connected to one or more further structural unit(s) selected from amino acids and amino acid analogues and other units whose molecular weight is no more than 270 and that are connected and interconnected by said types of bond(s) and/or bridges; forming a cyclic structure or cyclic structures in which the motif(s) Dd-Ee-Ff is/are the intermediary amino acid(s) and/or amino acid analogue(s) and/or are part(s) thereof, said cyclic structure(s) being defined by the the intermediary amino acids and other said constituents and bond(s) and/or bridge(s);

and wherein the number of the intermediary amino acid(s) and/or amino acid analogue(s) is preferably 3 to 9, and more preferably 3 to 6.

21. The targeting agent according to claim 20, wherein the number of the intermediary amino acid(s) and/or amino acid analogue(s) is 3.

22. The targeting agent according to any one of the previous claims, that comprises one or more cyclic structure(s) that comprises or that each comprise or one or more of which each comprise(s) a bond between a unit or residue XX and a unit or residue YY, by virtue of which bond the structure(s) is/are cyclic, and that has been made or can be formally considered as having been made by reacting XX and YY; wherein

XX is selected from the group of: amino acid residues, amino acid analogue residues, other structural units and residues whose molecular weight is no more than 270, and

each XX comprises at least one amino group or substituted amino group or substituted or unsubstituted hydrazine, hydrazide or hydrazone moiety, or an activated and/or protected form of any of these, that can participate and is participating in an amide, peptide, hydrazide and/or hydrazone bond or bridge, and

YY is selected from the group of: amino acid residues, amino acid analogue residues, other structural units and residues whose molecular weight is no more than 270, and

each YY comprises at least one carboxyl, activated carboxyl, ester, activated ester, acyl halide, *N*-carboxanhydride, carboxylic acid anhydride and/or related functional group, or an activated and/or protected form of any of these, that can participate and is participating in an amide, peptide, hydrazide and/or hydrazone bond or bridge

and wherein preferably, for each cyclic structure that has been made or can be formally considered as having been made by reacting XX and YY, independent of other cyclic structures if present,

XX comprises at least one amino group or substituted amino group or substituted or unsubstituted hydrazine, hydrazide or hydrazone moiety, or an activated and/or protected form of any of these, that is neither the alpha amino group nor an activated and/or protected form thereof; and/or

YY comprises at least one carboxyl, activated carboxyl, ester, activated ester, acyl halide, *N*-carboxanhydride, carboxylic acid anhydride and/or related functional group, or an activated and/or protected form of any of these, that is

neither the C-terminal carboxyl group nor an activated and/or protected form thereof.

and wherein more preferably, the cyclic structure(s) or one or more of them is/are made by reacting XX and YY or can be formally considered to have been made by reaction of XX and YY, and for each such cyclic structure, independently of other cyclic structure(s) if present, either XX or YY or both have been orthogonally and/or pseudoorthogonally and/or quasiorthogonally and/or semiorthogonally protected, in addition to possible other type(s) of protection that may or may not have been used,

and wherein still more preferably, one or more cyclic structure(s) have been made with the aid of two units selected from amino acids and amino acid analogues, one of which carried an orthogonally or quasiorthogonally or pseudoorthogonally protected amino group or an orthogonally or quasiorthogonally or pseudoorthogonally protected substituted amino group or an orthogonally or quasiorthogonally or pseudoorthogonally protected hydrazide moiety or an orthogonally or quasiorthogonally or pseudoorthogonally protected substituted hydrazide moiety, and the other one of which carried an orthogonally or quasiorthogonally or pseudoorthogonally protected carboxyl group.

23. The targeting agent according to any one of the previous claims, wherein:

the targeting unit or one or more of the targeting units comprise(s) one or more motifs selected from the group of: IRE, IRD, LRE, LRD, ERI, DRI, ERL, DRL, RIE, REI, IER, EIR, RLE, REL, LER, ELR, DIR, IDR, RDI, RID, DLR, LDR, RDL, RLD and structural and/or functional analogues thereof; wherein the amino acid residues I, L, R, E and D each can be, independently of the others, and in each case independently of other motif(s) if present, either in the L form or in the D form, and any other structural part(s)/unit(s) in the form of any optical isomer(s);

and wherein preferably:

the targeting unit or one or more of the targeting units comprise(s) one or more motifs selected from the group of: IRE, IRD, LRE, LRD, ERI, DRI, ERL and DRL and structural and/or functional analogues thereof; wherein the amino acid residues I, L, R, E and D each can be, independently of the others, and in each case independently of other motif(s) if present, either in the L form or in the D form, and any other structural part(s)/unit(s) in the form of any optical isomer(s).

24. The targeting agent according to any one of the previous claims, wherein the motif(s) Dd-Ee-Ff or one or more of them is/are selected from those indicated below in the Table, and/or from peptidyl and/or peptidomimetic analogues of those specific motif sequences, and preferably from those indicated on rows 1-16 of the Table, and/or from peptidyl and/or peptidomimetic analogues of the specific motif sequences indicated on said rows, and more preferably from those indicated on rows 1-8 of the Table, and/or from peptidyl and/or peptidomimetic analogues of the specific motif sequences indicated on said rows.

Table

	Aa/Dd	Bb/Ee	Cc/Ff
1	L-isoleucine	L-arginine	L-aspartic acid
2	"	"	L-glutamic acid
3	D-isoleucine	D-arginine	D-aspartic acid
4	"	"	D-glutamic acid
5	L-leucine	L-arginine	L-aspartic acid
6	"	"	L-glutamic acid
7	D-leucine	D-arginine	D-aspartic acid
8	"	"	D-glutamic acid
9	L-isoleucine	L-homoarginine	L-aspartic acid
10	"	"	L-glutamic acid
11	D-isoleucine	D-homoarginine	D-aspartic acid
12	"	"	D-glutamic acid
13	L-leucine	L-homoarginine	L-aspartic acid
14	"	"	L-glutamic acid
15	D-leucine	D-homoarginine	D-aspartic acid
16	"	"	D-glutamic acid
17	L-2-aminopentanoic acid	L-arginine	L-aspartic acid
18	D-2-aminopentanoic acid	D-arginine	D-aspartic acid
19	L-2-aminopentanoic acid	L-arginine	L-glutamic acid
20	D-2-aminopentanoic acid	D-arginine	D-glutamic acid
21	L-2-aminohexanoic acid	L-arginine	L-aspartic acid
22	D-2-aminohexanoic acid	D-arginine	D-aspartic acid
23	L-2-aminohexanoic acid	L-arginine	L-glutamic acid
24	D-2-aminohexanoic acid	D-arginine	D-glutamic acid
25	L-2-aminoheptanoic acid	L-arginine	L-aspartic acid
26	D-2-aminoheptanoic acid	D-arginine	D-aspartic acid
27	L-2-aminoheptanoic acid	L-arginine	L-glutamic acid
28	D-2-aminoheptanoic acid	D-arginine	D-glutamic acid
29	L-2-amino-2-ethylbutanoic acid	L-arginine	L-aspartic acid
30	D-2-amino-2-ethylbutanoic acid	D-arginine	D-aspartic acid
31	L-2-amino-2-ethylbutanoic acid	L-arginine	L-glutamic acid
32	D-2-amino-2-ethylbutanoic acid	D-arginine	D-glutamic acid
33	L-isoleucine	L-arginine	2-aminopropanedioic acid

34	D-isoleucine	D-arginine	"
35	L-leucine	D-arginine	"
36	D-leucine	D-arginine	"
37	L-isoleucine	L-arginine	L-2-aminohexanedioic acid
38	D-isoleucine	D-arginine	D-2-aminohexanedioic acid
39	L-leucine	L-arginine	L-2-aminohexanedioic acid
40	D-leucine	D-arginine	D-2-aminohexanedioic acid
41	L-isoleucine	L-arginine	L-2-aminoheptanedioic acid
42	D-isoleucine	D-arginine	D-2-aminoheptanedioic acid
43	L-leucine	L-arginine	L-2-aminoheptanedioic acid
44	D-leucine	D-arginine	D-2-aminoheptanedioic acid
45	L-2-aminopentanoic acid	L-homoarginine	L-aspartic acid
46	D-2-aminopentanoic acid	D-homoarginine	D-aspartic acid
47	L-2-aminopentanoic acid	L-homoarginine	L-glutamic acid
48	D-2-aminopentanoic acid	D-homoarginine	D-glutamic acid
49	L-2-aminohexanoic acid	L-homoarginine	L-aspartic acid
50	D-2-aminohexanoic acid	D-homoarginine	D-aspartic acid
51	L-2-aminohexanoic acid	L-homoarginine	L-glutamic acid
52	D-2-aminohexanoic acid	D-homoarginine	D-glutamic acid
53	L-2-aminoheptanoic acid	L-homoarginine	L-aspartic acid
54	D-2-aminoheptanoic acid	D-homoarginine	D-aspartic acid
55	L-2-aminoheptanoic acid	L-homoarginine	L-glutamic acid
56	D-2-aminoheptanoic acid	D-homoarginine	D-glutamic acid
57	L-2-amino-2-ethylbutanoic acid	L-homoarginine	L-aspartic acid
58	D-2-amino-2-ethylbutanoic acid	D-homoarginine	D-aspartic acid
59	L-2-amino-2-ethylbutanoic acid	L-homoarginine	L-glutamic acid
60	D-2-amino-2-ethylbutanoic acid	D-homoarginine	D-glutamic acid
61	L-isoleucine	L-homoarginine	2-aminopropanedioic acid
62	D-isoleucine	D-homoarginine	"
63	L-leucine	D-homoarginine	"
64	D-leucine	D-homoarginine	"
65	L-isoleucine	L-homoarginine	L-2-aminohexanedioic acid
66	D-isoleucine	D-homoarginine	D-2-aminohexanedioic acid
67	L-leucine	L-homoarginine	L-2-aminohexanedioic acid
68	D-leucine	D-homoarginine	D-2-aminohexanedioic acid
69	L-isoleucine	L-homoarginine	L-2-aminoheptanedioic acid
70	D-isoleucine	D-homoarginine	D-2-aminoheptanedioic acid
71	L-leucine	L-homoarginine	L-2-aminoheptanedioic acid
72	D-leucine	D-homoarginine	D-2-aminoheptanedioic acid

25. The targeting agent according to any one of the previous claims, wherein each motif comprising amino acids comprises only L amino acids or D amino

acids but not both, independently of the other motif(s) if present,

and/or

each motif comprising amino acids comprises only L amino acids,

and/or

each motif comprising amino acids comprises only D amino acids,

and/or

at least one motif Dd-Ee-Ff and/or targeting unit comprises L amino acids and at least one D amino acid,

and/or

at least one motif Dd-Ee-Ff and/or targeting unit comprises at least one beta amino acid and/or other amino acid that is not an alpha amino acid, and/or at least one amino acid and/or amino acid analogue that comprise(s) one or more unnatural side chain(s).

26. The targeting agent according to any one of the previous claims,

wherein the targeting unit or all of the targeting unit(s) comprise(s) one or more motif(s) selected from the group of: IRE, IRD, LRE, LRD, ERI, DRI, ERL, DRL, RIE, REI, IER, EIR, RLE, REL, LER, ELR, DIR, IDR, RDI, RID, DLR, LDR, RDL, RLD and structural and/or functional analogues thereof; preferably from the group of: IRE, IRD, LRE, LRD, ERI, DRI, ERL, DRL and structural and/or functional analogues thereof; more preferably from the group of: IRE, IRD, LRE, LRD, ERI, DRI, ERL and DRL; and

wherein the targeting unit or all of the targeting unit(s) comprise(s) also at least two amino acid residues selected from the group of cysteine and homocysteine, and wherein there is for each motif at least one cysteine or homocysteine residue either directly bonded to the aminoterminal amino acid of the motif or separated from it in the aminoterminal direction by 1 to 8 intermediary amino acid residues, and wherein there is for each motif at least one cysteine or homocysteine residue either directly bonded to the carboxyterminal amino acid of the motif or separated from it in the carboxyterminal direction by 1 to 8 intermediary amino acid residues; wherein the amino acid residues I, L, R, E and D each can be, independently of the others, and in each case independently of other motif(s) if present, either in the L form or in the D form and any other structural part(s)/unit(s) in the form of any optical isomer(s), and wherein the cysteine and/or homocysteine residues or some of them may or may not be in the oxidized (disulphide) form and the targeting unit(s) or one or more of them may or may not be cyclic.

27. The targeting agent according to any one of the previous claims, wherein

the targeting unit(s) or one or more of the targeting units and/or the motif(s) Dd-Ee-Ff and/or one or more of them is/are cyclic and/or comprise(s) one or more cyclic structure(s); and/or

the targeting unit(s) or one or more of the targeting units and/or the motif(s) Dd-Ee-Ff and/or one or more of them is/are cyclic so that the motif Dd-Ee-Ff or motifs Dd-Ee-Ff or one or more of the motif(s) Dd-Ee-Ff is/are included in one or more cyclic structures; and/or

the targeting unit(s) or one or more of the targeting units and/or the motif(s) Dd-Ee-Ff and/or one or more of them is/are non-cyclic and/or linear; and/or

the targeting unit(s) is/are or one or more of the targeting units and/or the motif(s) Dd-Ee-Ff and/or one or more of them are cyclic so that one or more motif(s) Dd-Ee-Ff is/are included in one or more cyclic structure(s) and one or more motif(s) Dd-Ee-Ff are not included in a cyclic structure or cyclic structures; and/or

the targeting unit(s) or one or more of them and/or the motif(s) Dd-Ee-Ff and/or one or more of them is/are cyclic, but no cyclic structure includes any disulphide bridge and/or one or more thiol groups are in the unoxidized -SH form; and/or

the targeting unit(s) and/or the motif(s) Dd-Ee-Ff is/are cyclic so that the motif Dd-Ee-Ff is or all of the motifs Dd-Ee-Ff is/are included in one or more cyclic structure(s).

28. The targeting agent according to any one of the previous claims, wherein

the targeting unit or one or more of the targeting units, preferably all of the targeting units, comprise(s) one or more motif(s) selected from the group of: IRE, IRD, LRE, LRD, ERI, DRI, ERL, DRL, RIE, REI, IER, EIR, RLE, REL, LER, ELR, DIR, IDR, RDI, RID, DLR, LDR, RDL, RLD and structural and/or functional analogues thereof; preferably from the group of: IRE, IRD, LRE, LRD, ERI, DRI, ERL, DRL and structural and/or functional analogues thereof; more preferably from the group of: IRE, IRD, LRE, LRD, ERI, DRI and ERL, DRL; and/or

wherein the targeting unit(s) or one or more of them, and preferably all of the targeting units, comprise(s) one or more sequence(s) selected from the group of: CIREC, CIRDC, CLREC, CLRDC, CERIC, CDRIC, CERLC, CDRLC, CRIEC, CREIC, CIERC, CEIRC, CRLEC, CRELC, CLERC, CELRC, CDIRC, CIDRC, CRDIC, CRIDC, CDLRC, CLDRC, CRDLC, CRLDC and structural and/or functional analogues thereof; preferably from the

group of: CIREC, CIRDC, CLREC, CLRDC, CERIC, CDRIC, CERLC, CDRLC and structural and/or functional analogues thereof; more preferably from the group of: CIREC, CIRDC, CLREC, CLRDC, CERIC, CDRIC, CERLC and CDRLC; and wherein optionally the structure(s) CIREC, CIRDC, CLREC, CLRDC, CERIC, CDRIC, CERLC, CDRLC, CRIEC, CREIC, CIERC, CEIRC, CRLEC, CRELC, CLERC, CELRC, CDIRC, CIDRC, CRDIC, CRIDC, CDLRC, CLDRC, CRDLC and CRLDC and structural and/or functional analogues thereof, and/or one or more of them may and/or may not be cyclic independently of each other; and/or the amount and/or location(s) of cyclic structure(s) may vary and/or change;

and wherein optionally the targeting unit or one or more of the targeting units comprise(s) one or more cyclic structure(s) so that said motif(s) or one or more of them is/are included in said cyclic structure or in one or more of said cyclic structures;

and wherein optionally the amino acid residues I, L, R, E and D each can be, independently of the others, and in each case independently of other motif(s) if present, either in the L form or in the D form, and any other structural part(s)/unit(s) in the form of any optical isomer(s);

and wherein optionally each motif Dd-Ee-Ff that comprises amino acids comprises only L amino acids or only D amino acids, independent of other possible motif(s); and wherein optionally the targeting unit(s) or one or more of the targeting units is/are cyclic because of a disulphide bond between the cysteine residues in each of one or more sequence(s) comprising one motif; and wherein optionally the targeting unit(s) or one or more of the targeting units is/are non-cyclic and/or partly non-cyclic and/or has/have variable and/or fluctuating and/or unknown and/or changing and/or undetermined and/or uncertain degree(s) of cyclicity.

29. The targeting agent according to any one of the previous claims, wherein the targeting unit or one or more of the targeting units comprise(s) one or more sequence(s) CIREC and/or CERIC and/or one or more structural and/or functional analogue(s) thereof.

30. The targeting agent according to any one of the previous claims, wherein

the cyclic structure or one or more of the cyclic structures comprise(s) one or more lactam structure(s) and/or one or more lactam-type structure(s) and/or one or more lactone structure(s) and/or one or more lactone-type structure(s) and/or one or more disulphide bridge(s); and/or

the cyclic structure or one or more of the cyclic structures comprise(s) one or more lactam structure(s) and/or one or more lactam-type structure(s) and/or one or more lactone structure(s) and/or one or more lactone-type structure(s); said structure or one or more of said structures being prepared with the aid of one or more amino acid(s) and/or amino acid analogue(s) and/or derivative(s) and/or protected and/or resin-bound and/or activated derivative(s) and/or analogue(s) thereof, that, in addition to the group(s) necessary and/or used for construction of a non-cyclic form or non-cyclic forms of the structure(s), comprise(s) one or more additional functional group(s) and/or their equivalent(s) that can be used for the synthesis/syntheses and/or spontaneous formation(s) of said cyclic structure(s) or one or more of them; and wherein optionally the additional functional group(s) and/or their equivalent(s) that can be used for the synthesis/syntheses and/or spontaneous formation(s) of said cyclic structure(s) or one or more of them, or one or more of said additional functional group(s) and/or their equivalent(s), is/are selected from the group of: amino, substituted amino, carboxyl, hydroxyl, and any resin-bound and/or protected and/or activated form(s) and/or modification(s) of amino, substituted amino, carboxyl and/or hydroxyl; and/or

the cyclic structure or one or more of the cyclic structures comprise(s) one or more lactam structure(s) and/or one or more lactam-type structure(s); said structure or one or more of said structures being prepared with the aid of one or more amino acid(s) and/or amino acid analogue(s) and/or derivative(s) and/or protected and/or resin-bound and/or activated and/or related derivative(s) and/or analogue(s) thereof, that, in addition to the group(s) necessary and/or used for construction of a non-cyclic form or non-cyclic forms of the structure(s), comprise(s) one or more additional functional group(s) and/or their equivalent(s) that can be used for the synthesis/syntheses and/or spontaneous formation(s) of said cyclic structure(s) or one or more of them; and wherein optionally the additional functional group(s) and/or their equivalent(s) that can be used for the synthesis/syntheses and/or spontaneous formation(s) of said cyclic structure(s) or one or more of them; or one or more of said additional functional group(s) and/or their equivalent(s), is/are selected from the group of: amino, substituted amino, carboxyl, and any resin-bound and/or protected and/or activated form(s) and/or modification(s) of amino, substituted amino and/or carboxyl; and/or

one or more orthogonally and/or quasiorthogonally and/or semiorthogonally and/or pseudoorthogonally protected amino acid(s) and/or amino acid analogue(s) and/or peptide(s) and/or peptide analogue(s), and/or one or more protected and/or activated and/or resin-bound and/or other bound and/or related form(s) of one or more of them, are used in one or more step(s) of the formation of the cyclic structure(s) or one or more of the cyclic

structures; and/or

one or more substance(s) and/or material(s) comprising one or more orthogonally and/or quasiorthogonally and/or semiorthogonally and/or pseudoorthogonally protected functional group(s) and/or their equivalent(s), is/are used, said protected functional group(s) and/or their equivalent(s) being selected from the group of: amino, substituted amino, and carboxyl; and/or

the cyclic structure(s) or one or more of the cyclic structures is/are made by spontaneous and/or assisted and/or catalyzed reaction between group A and group B, or between the reaction of two or more groups A with an equal number of groups B, wherein group(s) A is/are selected from the group of carboxyl, activated carboxyl and acyl halide, and group B is selected from the group of amino, substituted amino, activated amino, activated substituted amino, hydrazine, hydrazone, hydrazide, substituted and/or activated hydrazine, substituted and/or activated hydrazone, substituted and/or activated hydrazide and hydroxyl; and/or

the cyclic structure(s) or one or more of the cyclic structures is/are made by spontaneous and/or assisted and/or catalyzed reaction between group A and group B, or between the reaction of two or more groups A with an equal number of groups B, wherein group A and/or group B, or one or more of groups A and/or of groups B, is/are liberated from one or more orthogonally and/or quasiorthogonally and/or semiorthogonally and/or pseudoorthogonally protected functional group(s) and/or their equivalent(s) and one or more of them is/are or is/are not activated.

31. The targeting agent according to any one of the previous claims, wherein the targeting unit or one or more of the targeting units comprise(s):

one or more sequence(s) LRELSMGYFK and/or IQLRDWGFIL and/or one or more structural and/or functional analogues thereof, wherein optionally each of the amino acids other than G may be in the L form or in the D form, independently of other amino acids, and any other structural part(s)/unit(s) in the form of any optical isomer(s); and/or

LRE and/or LRD and/or one or more structural and/or functional analogues thereof, and also one or more GF and/or GY and/or GYF and/or GFY and/or one or more structural and/or functional analogue(s) thereof, and optionally also one or more residues selected from the group of: I, Q, L, W, S, M, G, Y, F, K and their structural and/or functional analogues; wherein optionally each of the amino acids other than G may be in the L form or in the D form, independently of other amino acids, and any other structural

part(s)/unit(s) in the form of any optical isomer(s).

32. The targeting agent according to any one of the previous claims, characterized in that

any cysteine and/or homocysteine residue(s) and/or other residue(s) and/or unit(s) comprising -SH that are present in the agent are in the unoxidized -SH form and not in the oxidized -S-S- form; and/or

any cysteine and/or homocysteine residue(s) and/or other residue(s) and/or unit(s) comprising -SH that are present in the targeting unit or targeting units or in one or more of them are in the unoxidized -SH form and not in the oxidized -S-S- form; and/or

one or more of the cysteine and/or homocysteine residue(s) and/or other residue(s) and/or unit(s) comprising -SH that are present in the targeting unit or targeting units or in one or more of them are in the unoxidized -SH form and not in the oxidized -S-S- form; and/or

at least one of the cysteine and/or homocysteine residue(s) and/or other residue(s) and/or unit(s) comprising -SH that are present in the targeting unit or targeting units or in one or more of them are in the unoxidized -SH form and not in the oxidized -S-S- form; and/or

any cysteine and/or homocysteine residue(s) and/or other residue(s) and/or unit(s) comprising -SH that are present in the agent are in the oxidized -S-S- form and not in the unoxidized -SH form;

any cysteine and/or homocysteine residue(s) and/or other residue(s) and/or unit(s) comprising -SH that are present in the targeting unit or targeting units or in one or more of them are in the oxidized -S-S- form and not in the unoxidized -SH form; and/or

at least two cysteine and/or homocysteine residue(s) and/or other residue(s) and/or unit(s) comprising -SH that are present in the targeting unit or targeting units or in one or more of them are in the oxidized -S-S- form and not in the unoxidized -SH form.

33. The targeting agent according to any one of the previous claims, wherein the targeting unit or targeting units or one or more of the them comprise one or more of the following: CyIRECyy, CyIRDCyy, CyLRECyy, CyLRDCyy, CyERICyy, CyDRICyy, CyERLCyy, CyDRLCyy, CyRIECyy, CyREICyy, CyIERCyy, CyEIRCyy, CyRLECyy, CyRELCyy, CyLERCyy, CyELRCyy, CyDIRCyy, CyIDRCyy, CyRDICyy, CyRIDCyy, CyDLRCyy, CyLDRCyy, CyRDLCyy or CyRLDCyy, and/or one or more structural and/or functional analogues thereof;

wherein Cy in each case independently means: homocysteine or cysteine; or another amino acid or amino acid analogue, or another structure with a formula/molecular weight no more than 270, comprising a thiol group or potentially comprising a thiol group or an oxidized thiol group; or an amino acid or an amino acid analogue, or another structure with a formula/molecular weight no more than 270, that is capable of forming a cyclic structure by reacting, as such and/or as activated and/or protected and/or deprotected, with Cyy, and Cyy means, independently in each case and independently of Cy: homocysteine or cysteine; or another amino acid or amino acid analogue, or another structure with a formula/molecular weight no more than 270, comprising a thiol group or potentially comprising a thiol group or an oxidized thiol group; or an amino acid or an amino acid analogue, or another structure with a formula/molecular weight no more than 270, that is capable of forming a cyclic structure by reacting, as such or as activated and/or protected and/or deprotected, with Cy, the reaction giving rise to the formation of a lactam or lactone or hydrazone-type or other cyclic structure;

or Cy and Cyy together mean a structural part or moiety that makes the structure cyclic;

and wherein any amino acid(s) may comprise L amino acid(s) and/or D amino acid(s); and the targeting agent, and/or targeting unit or units or one or more of them, may and/or may not be cyclic, and/or the amount and/or location(s) of cyclic structure(s) may vary and/or change.

34. The targeting agent according to any one of the previous claims, wherein the effector unit or the effector units or one or more of them, or part(s) of the effector unit(s) or of one or more effector unit(s) has/have one or more identical, similar and/or different useful and/or applicable and/or desired activity/activities and/or property/properties and/or their like, and/or can be converted to have it/them and/or one or more of them, and/or is/are converted to have it/them and/or one or more of them.

35. The targeting agent according to any one of the previous claims, wherein the effector unit or the effector units or one or more of them, or part(s) of the effector unit(s) or of one or more effector unit(s) has/have one or more identical, similar and/or different therapeutic and/or diagnostic, and/or therapeutically and/or diagnostically and/or for research purposes applicable and/or desired and/or potentially applicable, activity/activities and/or property/properties and/or their like, and/or can be converted to have it/them and/or one or more of them, and/or is/are converted to have it/them and/or one or more of them.

36. The targeting agent according to any one of the previous claims, wherein the effector

unit or the effector units or one or more of them, or part(s) of the effector unit(s) or of one or more effector unit(s):

has/have one or more identical, similar and/or different biological activity/activities; and/or

can be converted into one or more unit(s) that has/have or part(s) of which has/have a biological activity and/or more than one identical, similar and/or different biological activities; and/or

is/are converted into one or more unit(s) that has/have and/or part(s) of which has/have a biological activity and/or more than one identical, similar and/or different biological activities; and/or

has/have one or more identical, similar and/or different activity/activities and/or property/properties, that can be used directly or indirectly for detection and/or observation and/or qualitative analysis and/or quantitative analysis and/or other quantitation and/or signalling and/or imaging and/or photographing and/or other graphing and/or diagnosing and/or estimation and/or prediction and/or signal amplification and/or their like purpose(s) and/or for one or more procedures used for one or more of these purposes; and/or

can be converted, into one or more unit(s) that has/have an activity or property, or more than one identical, similar and/or different activities and/or properties, that can directly and/or indirectly be used for detection and/or observation and/or qualitative analysis and/or quantitative analysis and/or other quantitation and/or signalling and/or imaging and/or photographing and/or other graphing and/or diagnosing and/or estimation and/or prediction and/or signal amplification and/or their like purpose(s) and/or for one or more procedure(s) used for one or more of these purposes; and/or

is/are converted into one or more unit(s) that has/have and/or part(s) of which has/have an activity or property, or more than one identical, similar and/or different activity/activities and/or property/properties, that can directly and/or indirectly be used for detection and/or observation and/or qualitative analysis and/or quantitative analysis and/or other quantitation and/or signalling and/or imaging and/or photographing and/or other graphing and/or diagnosing and/or estimation and/or prediction and/or signal amplification and/or their like purpose(s) and/or for one or more procedure(s) used for one or more of these purposes; and/or

has/have the ability/abilities to bind to one or more preselected atom(s), molecule(s), part(s) of molecule(s) or ion(s), ion(s), structure(s), compound(s), substance(s), particle(s),

liposome(s), virus(es), other micro-organism(s), fragment(s) of cells and/or of micro-organism(s), cells, organelle(s), genetic material(s) and/or their functional and/or structural analogues such as phosphorothioates, and/or their like, and/or any preselected combination(s) of them, including combinations of identical, similar and/or different ones; and/or

is/are converted into one or more unit(s) that has/have and/or part(s) of which has/have the ability/abilities to bind to one or more preselected atom(s), molecule(s), part(s) of molecule(s) or ion(s), ion(s), structure(s), compound(s), substance(s), particle(s), liposome(s), virus(es), other micro-organism(s), fragment(s) of cells and/or of micro-organism(s), cells, organelle(s), genetic material(s) and/or their functional and/or structural analogues such as phosphorothioates, and/or their like, and/or any preselected combination(s) of them, including combinations of identical, similar and/or different ones.

37. The targeting agent according to any one of the previous claims, wherein the effector unit or the effector units or one or more of them, or part(s) of the effector unit(s) or of one or more effector unit(s)

can be converted, wholly or in part, from outside of the human and/or animal patient(s) and/or subject(s) and/or the sample(s) and/or other material(s) under study and/or treatment(s) and/or their like, and/or invasively with one or more apparatus(es), radiation(s), treatment(s) and/or material(s) and/or their like and/or by the administration(s) of one or more substance(s) and/or their like, and/or by any means into one or more unit(s) that have or one or more of which has/have and/or part(s) of which has/have a biological activity and/or more than one identical, similar and/or different biological activities;

and/or

is/are converted in the human or animal body or in a biological sample or other material, by the effect of the properties and/or enzymatic and/or other function(s) and/or conditions, such as pH and/or temperature and/or the aqueous milieu, and/or their like, into one or more unit(s) that has/have and/or part(s) of which has/have a biological activity and/or more than one identical, similar and/or different biological activities;

and/or

has/have one or more identical, similar and/or different activity/activities and/or property/properties, that can be used directly or indirectly for detection and/or observation and/or qualitative analysis and/or quantitative analysis and/or other quantitation and/or signalling and/or imaging and/or

photographing and/or other graphing and/or diagnosing and/or estimation and/or prediction and/or signal amplification and/or their like purpose(s) and/or for one or more procedures used for one or more of these purposes;

and/or

can be converted, wholly or in part, from outside of the human and/or animal patient(s) and/or subject(s) and/or the sample(s) and/or other material(s) under study and/or treatment(s) and/or their like, and/or invasively with one or more apparatus(es), radiation(s), treatment(s) and/or material(s) and/or their like and/or by the administration(s) of one or more substance(s) and/or their like, and/or by any means into one or more unit(s) that have or one or more of which has/have and/or part(s) of which has/have an activity or property, or more than one identical, similar and/or different activity/activities and/or property/properties, that can directly and/or indirectly be used for detection and/or observation and/or qualitative analysis and/or quantitative analysis and/or other quantitation and/or signalling and/or imaging and/or photographing and/or other graphing and/or diagnosing and/or estimation and/or prediction and/or signal amplification and/or their like purpose(s) and/or for one or more procedure(s) used for one or more of these purposes;

and/or

is/are converted in the human or animal body or in a biological sample or other material, by the effect of the properties and/or enzymatic and/or other function(s) and/or conditions, such as pH and/or temperature and/or the aqueous milieu, and/or their like, into one or more unit(s) that has/have and/or part(s) of which has/have an activity or property, or more than one identical, similar and/or different activity/activities and/or property/properties, that can directly and/or indirectly be used for detection and/or observation and/or qualitative analysis and/or quantitative analysis and/or other quantitation and/or signalling and/or imaging and/or photographing and/or other graphing and/or diagnosing and/or estimation and/or prediction and/or signal amplification and/or their like purpose(s) and/or for one or more procedure(s) used for one or more of these purposes;

and/or

has/have the ability/abilities to bind to one or more preselected atom(s), molecule(s), part(s) of molecule(s) or ion(s), ion(s), structure(s), compound(s), substance(s), particle(s), liposome(s), virus(es), other micro-organism(s), fragment(s) of cells and/or of micro-organism(s), cells, organelle(s), genetic material(s) and/or their functional and/or structural analogues such as phosphorothioates, and/or their like, and/or any preselected combination(s) of them, including combinations of identical, similar and/or

different ones;

and/or

is/are converted in the human or animal body or in a biological sample or other material, by the effect of the properties and/or enzymatic and/or other function(s) and/or conditions, such as pH and/or temperature and/or the aqueous milieu, and/or their like, into one or more unit(s) that has/have and/or part(s) of which has/have the ability/abilities to bind to one or more preselected atom(s), molecule(s), part(s) of molecule(s) or ion(s), ion(s), structure(s), compound(s), substance(s), particle(s), liposome(s), virus(es), other micro-organism(s), fragment(s) of cells and/or of micro-organism(s), cells, organelle(s), genetic material(s) and/or their functional and/or structural analogues such as phosphorothioates, and/or their like, and/or any preselected combination(s) of them, including combinations of identical, similar and/or different ones.

38. The targeting agent according to any one of claims 34 to 37, wherein the biological activity/activities and/or other said activity/activities and/or said property/properties and/or said ability/abilities to bind, of the effector unit or of the effector units or of one or more of them or of part(s) of the effector unit(s) or of part(s) of one or more effector unit(s), is/are different from and/or comprise(s) more than the selective binding of the targeting unit(s) and/or targeting agent(s) and/or targeting motif(s) according to this invention and/or the targeting function according to this invention; and/or is/are different from and/or comprise(s) more than the targeting function of the targeting unit(s) and/or the targeting agent(s) and/or the targeting motif(s) according to this invention and/or the targeting function according to this invention.

39. The targeting agent according to any one of the previous claims, wherein the effector unit(s) and/or part(s) of it/them is/are, directly and/or through and/or with the aid of one or more optional unit(s), conjugated, linked, coupled, bonded and/or bound to the targeting unit(s) and/or one or more of them.

40. The targeting agent according to any one of the previous claims, wherein the targeting agent comprises one or more unit(s) selected from the group of

- linker units,
- solubility modifier units,
- stabilizer units,
- charge modifier units,
- spacer units,
- lysis and/or reaction and/or reactivity modifier units,

- internalizing and/or internalization enhancer and/or membrane interaction units and/or other local route and/or local attachment/local binding and/or distribution affecting units,
- adsorption enhancer units, and
- other related units;

wherein optionally: one or more unit(s) has/have the properties and/or functions of more than one type of said units and/or one or more of said units has/have one or more property/properties and/or activity/activities of an effector unit and/or effector units.

41. The targeting agent according to any one of the previous claims, wherein the targeting unit itself or one or more of the targeting units, and/or part(s) thereof, is/are also an effector unit and/or constitute(s) more than one effector units and/or part(s) of one or more effector unit(s).

42. The targeting agent according to any one of the previous claims, wherein the linker unit(s) bind(s) or connect(s) to each other

one or more targeting unit(s)

and/or

one or more effector units

and/or

one or more identical and/or similar and/or different unit(s) selected from the group of:

- linker units,
- solubility modifier units,
- stabilizer units,
- charge modifier units,
- spacer units,
- lysis and/or reaction and/or reactivity modifier units,
- internalizing and/or internalization enhancer and/or membrane interaction units and/or other local route and/or local attachment/local binding and/or distribution affecting units,
- adsorption enhancer units, and
- other related units.

43. The targeting agent according to any one of the previous claims, wherein

the solubility modifier unit(s) enhance(s), decrease(s) and/or otherwise modify/modifies the solubility of the of the targeting agent and/or targeting unit(s) and/or their hydrolysis

product(s) and/or other products and/or part(s) of it/them; and/or

the stabilizer unit(s) stabilize(s) the structure of the targeting agent and/or targeting units(s) and/or their hydrolysis product(s) and/or part(s) of it/them; and/or

the charge modifier unit(s) increase(s), decrease(s) and/or otherwise modify/modifies the electrical charge(s) of the targeting agent, targeting units(s) and/or their hydrolysis product(s) and/or part(s) of it/them and/or one or more starting material(s) of it/them; and/or

the spacer unit(s) increase(s) the distance between specific units in the targeting agent and/or targeting unit(s) and/or its/their hydrolysis product(s) and/or part(s) of it/them and/or parts of its/their starting materials, and/or release(s) and/or decrease(s) steric hindrance and/or structural strain; and/or

the lysis and/or reaction and/or reactivity modifier unit(s) make(s) possible, and/or enhance(s) and/or make(s) more rapid and/or prevent(s) and/or inhibit(s) and/or make(s) more slow and/or quantitatively and/or qualitatively modifies/modify and/or change(s), and/or modifies/modify the course and/or products of, and/or alter(s) the prerequisites and/or optimal conditions of, and/or redirect(s), one or more hydrolytic and/or other lytic reaction(s) and/or other decomposition process(es) and/or reaction(s) and/or their continuation process(es) and/or reaction(s) of the targeting unit(s) and/or targeting agent and/or one or more starting material(s) and/or constituents thereof and/or one or more of their product(s) of hydrolysis and/or of other type(s) of lysis and/or of decomposition and/or of reaction(s); and/or

the lysis and/or reaction and/or reactivity modifier unit(s) increase(s) the susceptibility of the targeting agent and/or targeting unit(s) to one or more type(s) of enzymatic and/or non-enzymatic reaction(s) and/or process(es); and/or

the lysis and/or reaction and/or reactivity modifier unit(s) increase(s) the susceptibility of the targeting agent the hydrolysis of one or more effector unit(s); and/or

the internalizing unit(s) and/or internalization enhancer unit(s) and/or membrane interaction unit(s) and/or other local route and/or local attachment/local binding and/or distribution affecting unit(s) enhance(s) and/or make(s) more rapid and/or cause(s) and/or give(s) rise to and/or prevent(s) and/or inhibit(s) and/or affect(s) in one or more way(s) one or more process(es) that affect(s) and/or determine(s) and/or cause(s) and/or modifies/modify the route and/or fate and/or further localization in the vicinity of the

targeted area of the targeting agent and/or targeting unit(s) and/or product(s) of its/their hydrolysis and/or other lysis and/or decomposition and/or other reaction(s), and/or cause(s) the internalization of the targeting agent and/or targeting unit(s) and/or effector unit(s) and/or the binding of one ore more of them onto and/or into cell membranes after the targeting unit(s) and/or targeting agent have reacted their target(s); and/or

the adsorption enhancer unit(s) is/are such that it/they is/are not hydrolyzed or otherwise lost after absorption; and/or

the adsorption enhancer unit(s) is/are such that it/they is/are hydrolyzed off and/or otherwise lost after absorption.

44. The targeting agent according to any one of the previous claims, wherein the effector unit is or the effector units are or one or more effector unit(s) is/are selected from the group of:

- therapeutic agents and substances and related materials
- diagnostic agents and substances and related materials
- therapeutic agents and substances and related materials that can be used *in vivo*
- therapeutic agents and substances and related materials that can be used *in vitro*
- diagnostic agents and substances and related materials that can be used *in vivo*
- diagnostic agents and substances and related materials that can be used *in vitro*
- agents and substances and other materials that can be used for one or more research purposes
- agents and substances and other materials that can be used for cell sorting and/or enrichment and/or removal and/or their like
- agents and substances and other materials that can be wholly or in part be converted and/or are converted wholly or in part into one or more unit(s) mentioned in this list above and/or below
- agents and substances and other materials that have properties according to more than one point in this list above and/or below
- effector units having more than one usable and/or useful and/or applicable property/properties/activity/activities/their like
- pro-drug type analogues and derivatives and their like of any of the forementioned, and
- protected and partially protected and activated forms of any of the forementioned;
- nanodevices, microdevices, nanochips and their like

and/ or can bind one or more of the aforementioned;
and the targeting agent according to any one of the previous claims that comprises one or more effector unit(s) selected from said group above..

45. The targeting agent according to any one of the previous claims, wherein the effector unit is or the effector units are or one or more effector unit(s) is/are selected from the group of:

- therapeutic agents and substances and related materials
- diagnostic agents and substances and related materials
- cytostatic agents and substances and related materials
- cytotoxic agents and substances and related materials
- agents and substances and materials capable of affecting the cell cycle
- agents and substances and materials capable of affecting cell division
- antiangiogenic and/or related agents and substances, and related materials
- agents and substances and materials capable of affecting the cell division and/or metabolism and/or growth
- agents and substances and materials capable of affecting the cell viability directly and/or indirectly
- agents and substances and materials capable of affecting one or more immunological and/or host defence mechanism(s) and/or related phenomenon/phenomena and/or mechanism(s)
- agents and substances and materials capable of affecting immune cells and/or related cells and/or killer cells and/or their like
- agents and substances and materials capable of affecting apoptosis and/or one or more phenomena affecting and/or preventing and/or enhancing apoptosis and/or related mechanism(s)
- radioactive nuclei and molecules and ions and chemical structures and clusters and particles and other materials comprising one or more type(s) of them
- magnetic atoms and molecules and ions, and chemical structures and clusters and particles and other materials comprising one or more type(s) of them
- paramagnetic atoms and molecules and ions, and chemical structures and clusters and particles and other materials comprising one or more type(s) of them
- ferromagnetic atoms and molecules and ions, and chemical structures and clusters and particles and other materials comprising one or more type(s) of them
- ferrimagnetic atoms and molecules and ions, and chemical structures and clusters and particles and other materials comprising one or more type(s) of them
- enzyme(s)
- protein(s)
- avidins and related materials
- biotin and related materials
- transferrins and related materials
- anthracyclines and their derivatives and analogues and related substances

- daunorubicin, doxorubicin and their like
- histidine tags and cysteine tags and related materials and tags and related structures of any type including structures comprising unnatural parts and/or constituents
- substances, molecules, atoms, ions and other materials easily and/or potentially detectable by one or more methods and/or visually and/or using methods, apparatuses and/or substances and/or organoleptically
- fluorescent substances and molecules and their like
- phosphorescent substances and molecules and their like
- chemiluminescent substances and molecules and their like and substances and materials useable for chemiluminescent method(s)
- bioluminescent substances and molecules and their like and substances and materials useable for bioluminescent method(s)
- nucleic acids and other genetic matereials and related materials
- DNA
- RNA
- PNA (peptide nucleic acid)
- antisense oligonucleotides and other antisense materials and related substances
- phosphorothioates and their like
- chelates
- chelating agents
- metal complexes
- vasoconstrictors and related substances
- pain reliefing agents and related substances
- circulation modifying agents and related substances
- cytokines and related substances
- interferons and related substances
- interleukins and related substances
- prostaglandins and related substances
- antineoplastic agents and substances and and related materials of any type
- alkaloids
- antitumor alkaloids
- vinca alkaloids
- vincristine and related materials
- vinblastine and related materials
- bleomycins and related materials
- metal bleomycins and related materials
- copper bleomycins and related materials
- iron bleomycins and related materials
- taxol and related materials

- paclitaxel and related materials
- metal atoms and ions and molecules and atoms and ions and other materials comprising one or more metal atoms and/or ions and/or clusters and/or particles and/or solvates and/or metal(s) in any form and amount
- platinum atoms, ions and compounds and particles and solvates and any type and amount of platinum
- copper atoms, ions and compounds and particles and solvates and any type and amount of copper
- iron atoms, ions and compounds and particles and solvates and any type and amount of iron
- any transition metal atoms, ions and compounds and particles and solvates and any type and amount of any transition metal(s)
- rare earth metal atoms, ions and compounds and particles and solvates and any type and amount of any rare eart metal(s)
- gadolinium atoms, ions, complexes, compounds, particles and solvates and any type and amount of gadolinium
- europium atoms, ions, complexes, compounds, particles and solvates and any type and amount of europium
- technetium nuclei, atoms, ions, complexes, compounds, particles and solvates and any type and amount of technetium
- Indium nuclei, atoms, ions, complexes, compounds, particles and solvates and any type and amount of Indium
- artificial element nuclei and other artificial nuclei, atoms, ions and compounds and particles and solvates and any type and amount of artificial element(s) and/or nuclei
- copper chelates and complexes
- copper(II) chelates and complexes
- copper(I) chelates and complexes
- copper(III) chelates and complexes
- platinum chelates and complexes
- platinum(II) chelates and complexes
- platinum(IV) chelates and complexes
- cisplatin, carboplatin and their analogues, derivatives and related substances
- *trans*-bis(salicylaldoximato)copper(II) and its derivatives and anlogues and related substances
- *trans*-bis(salicylaldoximato)-type metal complexes and their derivatives and anlogues and related substances
- salicylaldoxime and its analogues and derivatives and salicylaldehyde hydrazones and their analogues and derivatives, and related materials and substances, and metal complexes of any of said materials

- *trans*-bis(salicylaldoximato)copper(II) and its derivatives and anlogues and related substances, comprising one or more radioactive copper nucleus/nuclei and/or one or more other radioactive nucleus/nuclei
- *trans*-bis(salicylaldoximato)-type metal complexes and their derivatives and anlogues and related substances comprising one or more radioactive nucleus/nuclei
- salicylaldoxime and its analogues and derivatives and salicylaldehyde hydrazones and their analogues and derivatives, and related materials and substances, and metal complexes of any of said materials; and forms of any of these comprising one or more radioactive nucleus/nuclei
- bis(thiosemicarbazone)s and their analogues and derivatives and copper chelates thereof and other metal chelates thereof, and radioactive forms thereof
- bis(guanylhydrazone)s
- polyamine antimetabolites and anlogues and derivatives and inhibitors of their uptake and substances taken up by cells by the mechanism(s) used for polyamine uptake
- asparaginases
- hydrolytic enzymes
- clotting substances and their like
- thrombotic substances and substances capable of causing and/or affecting thrombosis
- substances capable of collecting and/or absorbing external radiant energy and/or other external energy, and related materials
- substances, materials, atoms, ions, molecules and their like usable for positron emission
- substances, materials, atoms, ions, molecules and their like usable for positron emission tomography and/or related method(s)
- substances, materials, atoms, ions, molecules and their like usable for one or more diagnostic methodology/methodologies and/or technique(s)
- substances, materials, atoms, ions, molecules and their like usable for one or more nuclear magnetic resonance methodology/methodologies and/or technique(s)
- substances, materials, atoms, ions, molecules and their like usable for one or more magnetic resonance methodology/methodologies and/or technique(s)
- substances, materials, atoms, ions, molecules and their like usable for one or more nuclear magnetic resonance diagnostic methodology/methodologies and/or technique(s)
- substances, materials, atoms, ions, molecules and their like usable for one or more magnetic resonance diagnostic methodology/methodologies and/or technique(s)
- substances, materials, atoms, ions, molecules and their like usable for one or more magnetic resonance spectroscopic methodology/methodologies and/or technique(s)
- substances, materials, atoms, ions, molecules and their like usable for one or more nuclear magnetic resonance spectroscopic methodology/methodologies and/or technique(s)
- substances, materials, atoms, ions, molecules and their like usable for one or more electron paramagnetic and/or electron spin resonance spectroscopic

methodology/methodologies and/or technique(s)
- substances, materials, atoms, ions, molecules and their like usable for one or more magnetic resonance spectroscopic methodology/methodologies and/or technique(s)
- substances, materials, atoms, ions, molecules and their like usable for one or more nuclear magnetic resonance spectroscopic methodology/methodologies and/or technique(s)
- substances, materials, atoms, ions, molecules and their like usable for one or more electron paramagnetic and/or electron spin resonance spectroscopic methodology/methodologies and/or technique(s)
- alkylating agents and their analogues and substances with a related mechanism of action or related mechanismof action, and related materials
- radioactive nuclei/substances capable of emitting alpha radiation
- radioactive nuclei/substances capable of emitting beta radiation
- radioactive nuclei/substances capable of emitting gamma radiation
- radioactive nuclei/substances capable of emitting positron radiation
- radioactive nuclei/substances capable of emitting radiation
- radioactive nuclei/substances capable of emitting any type of radiation
- nuclei/substances capable of emitting any type of radiation other than radioactive substances
- nuclei/substances capable of absorbing radiation
- nuclei/substances capable of absorbing any type of radiation
- nuclei/substances/molecules/ions/elements/enriched elements and their compounds and ions and other forms, that are usable for neutron capture therapy and/or diagnostic method(s) based based on neutron capture
- nuclei/substances/molecules/ions/elements/enriched nuclei and their compounds and ions and other forms, that are usable for boron and/or gadolinium and/or litium neutron capture therapy and/or diagnostic method(s) based based on neutron capture
- compounds and other materials and substances comprising boron and/or litium and/or gadolinium and/or enriched and/or specific isotope(s)/nuclei thereof
- NMR relaxation agents and their like
- nitroxyl radicals and/or other semistable/stable radicals
- NMRI relaxation agents and their like
- NMR relaxation enhancing agents and their like
- cobalt ions and/or atoms and/or complexes
- manganese ions and/or atoms and/or complexes
- iron ions and/or atoms and/or complexes
- nickel ions and/or atoms and/or complexes
- platinum ions and/or atoms and/or complexes
- palladium ions and/or atoms and/or complexes
- toxic substances

- inhibitors of metabolism and antimetabolites and their like
- pyridoxal kinase inhibitors
- protein kinase inhibitors
- substances interfering with and/or inhibiting cell signalling and/or cell-to-cell and/or cell-matrix interaction(s) and/or their like
- enzyme inhibitors
- adenosylmethionine decarboxylase inhibitors
- arginine decarboxylase inhibitors
- ornithine decarboxylase inhibitors
- aquaporins and their like
- ion channels and their like and substances interfering with them and/or their function and/or inhibiting and/or enhancing and/or changing their activity/properties/functien, and/or related substances
- antibodies and their parts and fragments and their like and substances comprising such
- boron and isotope-enriched boron and substances comprising such
- NMR active nuclei and substances comprising such
- enriched NMR active nuclei and substances comprising such
- enriched carbon-13 and substances comprising it
- UV-absorbing agents and substances and their like
- visible light-absorbing agents and substances and their like
- NMR active nuclei
- carboranes
- carboranes comprising isotope-enriched boron
- carboranes-type compounds
- carboranes-type compounds comprising isotope-enriched boron
- podophyllum derivatives and their like
- folic acid analogues and their like
- purine and/or pyrimidine anlogues and their like
- nitrosoureas and their like
- androgens and their like
- antiandrogens and their like
- estrogens and their like
- antiestrogens and their like
- corticosteroids and their like
- triazine type compounds and their like
- ethyleneimine derivatives and their like
- nitrogen mustards and their like
- plant toxins, fish toxins, marine toxins animal toxins and their like
- venom constituents and their like

- alkyl sulfonates and related substances
- steroid synthesis inhibitors
- receptor antagonists and agonists and their like
- ethylediammine tetraacetic acid and its analogues and derivatives and their like and ionic forms thereof, and metal complexes of any of these
- polycarboxylic acids and their like and their metal chelates
- reactive substances such as oxidants, reducing agents, precipitating agents, specific oxidants, acyl halides, acid anhydrides, bases, acidic substances, hypochlorites, ozonides, molozonides, and liberators thereof, and any materials of related types
- membrane disrupting agents and other substances interfering with biological membranes and/or related structures, and their like
- polyamine-type compounds and their metal complexes
- dendrimeric compounds and their analogues and derivatives, and metal complexes thereof
- dendrimeric compounds and their analogues and derivatives, that comprise one or more of the substances and/or materials and so on listed in this list above
- analogues of the forementioned or one or more thereof
- derivatives of the forementioned or one or more thereof
- pro-drug type analogues and derivatives and their like of any of the forementioned
- protected and partially protected forms of any of the forementioned, and
- other related materials and their like;

and,

the targeting agent according to any one of the previous claims that comprises one or more effector unit(s) selected from said group.

45. The targeting agent according to any one of the previous claims, wherein the effector unit or at least one effector unit has more than one type of useful activity and/or property and/or effect and/or ability and/or action and/or use and/or their like; and/or there are at least two effector units and the effector units or some of them, altogether, have more than one type of useful activity and/or property and/or effect and/or ability and/or action and/or use and/or their like.

46. The targeting agent according to any one of the previous claims that has one or more diagnostic application(s), use(s) and/or their like and also has one or more therapeutic application(s) and/or use(s) and/or their like and optionally may have one or more other use(s), application(s) and/or their like.

47. The targeting agent according to any one of the previous claims, that comprises one or

more linker unit(s) and/or effector unit(s) and or other unit(s) that can, directly and/or after deprotection(s) and/or activation(s) and/or their like and/or after modification(s), be linked and/or connected and/or bonded and/or bound and/or coupled to/with one or more identical and/or similar and/or different unit(s), and/or will spontaneously and/or enzymatically and/or otherwise, directly and/or after deprotection(s) and/or activation(s) and/or their like and/or after modification(s) and/or spontaneous and/or enzymatic and/or their like deprotection(s) and/or activation(s) and/or their like, be linked and/or connected and/or bonded and/or bound and/or coupled to/with one or more identical and/or similar and/or different unit(s).

48. The targeting agent according to any one of the previous claims, wherein the unit(s) or one or more of the units to be linked to the targeting agent or unit are and/or comprise effector unit(s) and/or spacer unit(s) and/or linker unit(s), and/or combination(s) of these, and/or protected and/or activated and/or pro-drug-type and/or other form(s) thereof.

49. The targeting agent according to any one of the previous claims;

that is/has been, and/or can and/or will and/or is intended to be and/or become, linked and/or connected and/or bonded and/or bound and/or coupled;
and/or the linker and/or spacer and/or effector unit(s) and/or other unit(s) and/or structural part(s) of which, and/or one or more of the linker and/or spacer and/or effector unit(s) and/or other unit(s) and/or structural part(s) of which, is/are/has been/have been, and/or is/are intended to be and/or become, linked and/or connected and/or bonded and/or bound and/or coupled:

to/with more than one identical and/or similar and/or different unit(s), and/or

to/with several identical and/or similar and/or different unit(s), and/or

with the aid of one or more dendrimer/dendrimeric and/or its/their like structure(s)/fragment(s)/their like to/with several identical and/or similar and/or different unit(s), and/or

to/with several identical and/or similar and/or different unit(s) so, that the targeting agent can be considered as being a dendrimeric structure and/or has been constructed and/or designed and/or synthesized in a way typical of dendrimeric structures,

and/or that has a dendrimer-type and/or multivalent and/or polyvalent structure and/or

binding/bonding/linking/connection/coupling ability and/or capacity and/or their like and/or resembles that kind of structure(s),

and/or that can and/or will be/become linked and/or connected and/or bonded and/or bound and/or coupled to/with several identical and/or similar and/or different unit(s) and can be used and/or is intended for binding/bonding/linking/connection/coupling at least three effector unit(s) and/or other unit(s),

and/or that can and/or will be linked and/or connected and/or bonded and/or bound and/or coupled to/with several identical and/or similar and/or different unit(s) and can be used and/or isintended for binding/bonding/linking/connection/coupling at least three effector unit(s) and/or other unit(s) and/or for amplification of binding, detection, observation, biological effect(s) and/or one or more desired activity/activities/property/properties/effect(s)/function(s) and/or their like.

50. A targeting unit according to what is defined for a targeting unit in any one of the previous claims, and any salt(s), ester(s), amide(s), hydrazide(s), *N*-substituted amide(s), *N*-substituted hydrazide(s), hydroxamic acid -type derivative(s), *C*-terminally decarboxylated analogue(s), *N*-substituted derivative(s), and any related analogue(s) and/or derivative(s), and/or their combination(s), of one or more of such targeting units.

51. A targeting unit that comprises:

one or more identical, similar and/or different motif(s) Dd-Ee-Ff as defined in any one of the previous claims, and/or one or more identical, similar and/or different targeting unit(s) as defined in any one of the previous claims, and/or one or more identical, similar and/or different peptide sequence(s) and/or structural and/or functional analogue(s) thereof as defined in any one of the previous claims;

and/or that is and/or comprises one or more salt(s), ester(s), amide(s), hydrazide(s), *N*-substituted amide(s), *N*-substituted hydrazide(s), hydroxamic acid -type derivative(s), *C*-terminally decarboxylated analogue(s), *N*-substituted derivative(s), and/or any related analogue(s) and/or derivative(s), and/or their combination(s), of one or more of them.

52. A targeting unit that comprises one or more identical, similar and/or different motif(s)

Dd-Ee-Ff

and/or one or more salt(s), ester(s), amide(s), hydrazide(s), *N*-substituted amide(s), *N*-substituted hydrazide(s), hydroxamic acid -type derivative(s), *C*-terminally decarboxylated analogue(s), *N*-substituted derivative(s), and/or any related analogue(s) and/or derivative(s), and/or their combination(s), of one or more such motif(s),

wherein

Dd is either Aa or Bb or Cc or Aa′ or Bb′ or Cc′, and
Ee is either Aa or Bb or Cc or Aa′ or Bb′ or Cc′, and
Ff is either Aa or Bb or Cc or Aa′ or Bb′ or Cc′, and
Dd-Ee-Ff comprises Aa/Aa′and Bb/Bb′ and Cc/Cc′, and

wherein

Aa is the L- or D- form of isoleucine, leucine, *tert*-leucine or valine, or a structural and/or functional analogue thereof comprising in its side chain a branched, non-branched and/or alicyclic structure with at least two similar or different atoms selected from the group of carbon atoms, silicon atoms, halogen atoms bonded to one or more carbon(s), ether-oxygens and thioether-sulphurs;

Bb is the L- or D- form of arginine, homoarginine or canavanine, or a structural and/or functional analogue thereof comprising at least one guanyl and/or amidino group or a related group that has or can through protonation obtain a delocalized positive charge;

Cc is the L- or D- form of glutamic acid or aspartic acid, or a structural and/or functional analogue thereof, comprising in its side chain at least one carboxyl group or esterified carboxyl group;

Aa′ is a branched or non-branched or cyclic non-aromatic, lipophilic and/or hydrophobic amino acid or amino acid analogue or derivative or a structural and/or functional analogue thereof, or an amino acid or carboxylic acid or amino acid analogue or derivative or carboxylic acid analogue or derivative that has one or more lipophilic carborane-type and/or other lipophilic boron-containing side chain(s) or its/their equivalent(s) or another lipophilic cage-type structure;

Bb′ is an amino acid or amino acid analogue or derivative or a structural and/or functional analogue thereof, that comprises one or more guanyl

group(s) and/or amidino group(s) and/or its/their analogue(s) and/or derivative(s) and/or structural and/or functional equivalent(s) and/or one or more group(s) that comprise(s) at least two nitrogen atoms each and has/have or can gain a delocalized positive charge;

Cc′ is an amino acid or amino acid analogue or derivative or a structural and/or functional analogue thereof that comprises: one or more side-chain carboxyl group(s) and/or esterified carboxyl group(s), and/or ketoxime and/or aldoxime and/or hydroxamic acid group(s) and/or ketone- and/or aldehyde-carbonyl(s),

and/or the motif(s) Dd-Ee-Ff or one or more of them is/are structural and/or functional analogue(s) of a structure or structures where Dd-Ee-Ff is as defined above;

and/or the targeting unit comprises one or more of the following:

- any salt(s)
- any ester(s)
- any amide(s)
- any hydrazide(s)
- any *N*-substituted amide(s)
- any *N*-substituted hydrazide(s)
- any hydroxamic acid derivative(s)
- any decarboxylated analogue(s)
- any *N*-substituted derivative(s)
- any other related derivative(s)
- any other related analogue(s)
- any combination of any of such salt, derivative and/or analogue types,

of the targeting unit as defined above.

53. The targeting unit according to any one of claims 50 to 52, characterized in that it exhibits selective binding to one or more type(s) of: tumors and/or cancer(s) and/or tumor cells and/or cancer cells and/or malignant cells and/or transformed cells and/or tumor tissues and/or cancer tissues and/or malignant tissues and/or transformed tissues and/or leukemia cells and/or malignant blood cells and/or tranformed blood cells and/or related cells and/or tissues and/or tumor endothelium and/or activated endothelium and/or angiogenic endothelium and/or tumor-endothelium cells and/or activated-endothelium cells and/or angiogenic endothelium cells, and/or their like.

54. The targeting unit according to any one of claims 50 to 53, characterized in

that it exhibits selective binding to one or more type(s) of: tumors and/or cancer(s) and/or tumor cells and/or cancer cells and/or malignant cells and/or transformed cells and/or tumor tissues and/or cancer tissues and/or malignant tissues and/or transformed tissues and/or leukemia cells and/or malignant blood cells and/or tranformed blood cells and/or related cells and/or tissues and/or tumor endothelium and/or activated endothelium and/or angiogenic endothelium and/or tumor-endothelium cells and/or activated-endothelium cells and/or angiogenic endothelium cells, and/or their like, *in vivo* and/or *in vitro* and/or *ex vivo* and/or *in situ*.

55. The targeting unit according to any one of claims 50 to 54, characterized in that it exhibits selective binding to one or more type(s) of: tumors and/or cancer(s) and/or tumor cells and/or cancer cells and/or malignant cells and/or transformed cells and/or tumor tissues and/or cancer tissues and/or malignant tissues and/or transformed tissues and/or leukemia cells and/or malignant blood cells and/or tranformed blood cells and/or related cells and/or tissues and/or tumor endothelium and/or activated endothelium and/or angiogenic endothelium and/or tumor-endothelium cells and/or activated-endothelium cells and/or angiogenic endothelium cells, and/or their like, *in vivo*.

56. The targeting unit according to any one of claims 50 to 55, characterized in that it exhibits selective binding to one or more type(s) of: tumors and/or cancer(s) and/or tumor cells and/or cancer cells and/or malignant cells and/or transformed cells and/or tumor tissues and/or cancer tissues and/or malignant tissues and/or transformed tissues and/or leukemia cells and/or malignant blood cells and/or tranformed blood cells and/or related cells and/or tissues and/or tumor endothelium and/or activated endothelium and/or angiogenic endothelium and/or tumor-endothelium cells and/or activated-endothelium cells and/or angiogenic endothelium cells, and/or their like, *in vitro* and/or *ex vivo*.

57. The targeting unit according to any one of claims 50 to 56, that is capable of binding to one or more type(s) of: primary tumors and/or cancers, and/or tumor/cancer endothelium, and/or tumor/cancer metastases, and/or residive/residual tumors and/or cancers, and/or recurred/recurrent/relapsed tumors and/or cancers, and/or tumor cells; *in vivo* and/or *in vitro* and/or *ex vivo* and/or *in situ*.

58. The targeting unit according to any one of claims 50 to 57,

that is cyclic and/or forms part(s) of one or more cyclic structure(s); and/or

that is not cyclic and does not form part(s) of a cyclic structure or cyclic structures; and/or

that is linear; and/or

is/are branched and/or is/are not branched and/or is/are branched and cyclic; and/or

wherein the amount and/or location(s) of cyclic structure(s) may vary and/or change, and/or be in a state of equilibrium and/or fluctuation and/or related phenomenon/phenomena, and/or be uncertain and/or indifferent and/or undetermined, and/or wherein the degree of cyclicity at any potentially cyclic location may be partial and/or may be essentially total and/or may be essentially none and/or may be variant;

that and/or one or more part(s) of which may be cyclic and/or may not be cyclic, and wherein the amount and/or location(s) of cyclic structure(s) may vary and/or change.

59. The targeting unit according to any one of claims 50 to 58, that comprises more than one motif Dd-Ee-Ff, wherein the motif(s) Dd-Ee-ff may be identical and/or similar and/or different and/or overlapping.

60. The targeting unit according to any one of claims 50 to 59, wherein the motif(s) Dd-Ee-Ff is/are selected from the group of

Aa/Aa′- Bb/Bb′- Cc/Cc′,
Aa/Aa′- Cc/Cc′- Bb/Bb′,
Bb/Bb′- Aa/Aa′- Cc/Cc′,
Bb/Bb′- Cc/Cc′- Aa/Aa′,
Cc/Cc′- Aa/Aa′- Bb/Bb′ and
Cc/Cc′- Bb/Bb′- Aa/Aa′,

preferably from the group of

Aa/Aa′- Bb/Bb′- Cc/Cc′ and
Cc/Cc′- Bb/Bb′- Aa/Aa′.

61. The targeting unit according to any one of claims 50 to 60, wherein the motif(s) Dd-Ee-Ff or one or more of them is/are

Aa/Aa′- Bb/Bb′- Cc/Cc′.

62. The targeting unit according to any one of claims 50 to 61, wherein the motif(s) Dd-Ee-Ff or one or more of them is/are selected from the group of

Aa-Bb-Cc,
Aa-Cc-Bb,
Bb-Aa-Cc,
Bb-Cc-Aa,
Cc-Aa-Bb and
Cc-Bb-Aa,

preferably from the group of

Aa-Bb-Cc and
Cc-Bb-Aa.

63. The targeting unit according to any one of claims 50 to 62, wherein the motif(s) Dd-Ee-Ff or one or more of them is/are

Aa-Bb-Cc.

64. The targeting unit according to any one of claims 50 to 63,

wherein the targeting unit is is cyclic and/or form(s) part(s) of one or more cyclic structure(s) in such a way that the motif(s) and/or one or more of them is/are included in one or more cyclic structure(s); and/or

wherein the cyclic structure(s) or one or more of them is/are formed through one or more peptide bond(s) and/or other amide bond(s) and/or disulphide bond(s) and/or ester bonds; and/or

wherein the cyclic structure(s) or one or more of them comprise(s) at least one lactone and/or a lactame bond; and/or

wherein the cyclic structure(s) or one or more of them comprise(s) at least one disulphide bond; and/or

wherein the cyclic structure(s) or one or more of them is/are formed through one or more hydrazone and/or one or more hydrazide moiety/moieties and/or comprises one or more C-N-N-C and/or C=N-N=C and/or C-N-N=C and/or C-N=N-C moiety/moieties.

65. The targeting unit according to any one of claims 50 to 64, that comprises two or more

identical and/or similar and/or different motifs Dd-Ee-Ff.

66. The targeting unit according to any one of claims 50 to 65, that comprises one or more structure(s)

Kk-Dd-Ee-Ff-Ll

wherein

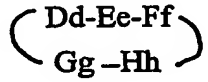
the motif(s) Dd-Ee-Ff is/are as defined in claim 1 and/or in claim 52 and/or in any other one(s) of the previous claims, and Kk and Ll, independently of each other, each comprise one or more structural fragment(s) and/or functional group(s) that can be used to form a bond and/or linkage between Kk and Ll so that a cyclic structure is formed, or Kk and Ll are parts of a structure so that Kk-Dd-Ee-Ff-Ll is cyclic;

and/or

the motif(s) Dd-Ee-Ff is/are as defined in claim 1 and/or in claim 52 and/or in any other one(s) of the previous claims, and Kk and Ll, independently of each other, each comprise one or more structural fragment(s) and/or functional group(s) that can be used to form: a lactame structure, or a lactam-type structure, or a lactone structure, or a lactone-type structure, or a cyclic structure comprising a cystine, or a cyclic structure comprising a cystine-type structure, or a cyclic structure comprising another disulphide bridge, or a hydrazone- and/or hydrazide-type bridge or related type of bridge; between Kk and Ll so that a cyclic structure is formed; and/or

the motif(s) Dd-Ee-Ff is/are as defined in claim 1 and/or in claim 52 and/or in any other one(s) of the previous claims, and Kk and Ll are parts of a lactone and/or a lactone-type structure, and/or a cyclic structure comprising a cystine, and/or a cyclic structure comprising a cystine-type structure, or a cyclic structure comprising another disulphide bridge; so that Kk-Dd-Ee-Ff-Ll is cyclic.

67. The targeting unit according to any one of claims 50 to 66, wherein the cyclic structure(s) or one or more of them is/are



wherein Gg–Hh is/are selected from the group of:

(a) cystine (i.e., Gg and Hh are cysteines that are connected to each other with

a disulphide bridge);
(b) two amino acids directly connected to each other via a peptide bond;
(c) two amino acid analogues connected to each other via a peptide bond;
(d) more than two amino acid(s) and/or amino acid analogue(s) connected to each other via one or more peptide bond(s) and/or amide bond(s) and/or one or more disulphide bridge(s);
(e) a cystine-type structure where Hh and Gg independently of each other are either an amino acid or another structure that comprises an 'oxidized thiol' moiety and a disulphide bridge existing between them; and
(f) two structures comprising each maximally 20 non-hydrogen atoms and an unlimited number of hydrogen atoms, either one or both of which are/is not an amino acid, connected to each other with a peptide bond.

68. The targeting unit according to any one of claims 50 to 67, that comprises 3 to 40, preferably 3 to 15, more preferably 3 to 8, amino acid(s) and/or structural and/or functional analogue(s) of amino acid(s).

69. The targeting unit according to any one of claims 50 to 68, wherein

the motif Dd-Ee-Ff or each one of the motifs Dd-Ee-Ff forms part of a structure comprising at least two units of cysteine and/or homocysteine and/or other amino acid(s) and/or amino acid analogue(s) comprising a thiol (-SH) group each, preferably units of cysteine, that are spaced apart by a number of 3 to 20, preferably 3 to 9, more preferably 3 to 6, intermediary amino acid(s) and/or amino acid analogue(s) and interconnected by a disulphide bond, forming a cyclic structure or cyclic structures in which the motif(s) Dd-Ee-Ff is/are formed by the intermediary amino acid(s) and/or amino acid analogue(s), said cyclic structure(s) being defined by the cysteine unit(s), homocysteine unit(s) and/or other amino acid and/or amino acid analogue unit(s) comprising a thiol (-SH) group each, the intermediary amino acid(s) and/or amino acid analogue(s) and the disulphide bond; and/or

wherein the motif Dd-Ee-Ff forms or each one of the motifs Dd-Ee-Ff form or one or more of them each form(s) part of a structure comprising, in addition to the motif(s) Dd-Ee-Ff: two units of amino acid(s) and/or amino acid analogue(s) and/or other type(s) of molecule(s) and/or fragment(s) whose individual molecular weight is no more than 270; that are spaced apart by a number of 3 to 20, preferably 3 to 9, more preferably 3 to 6, intermediary amino acid(s) and/or amino acid analogue(s); and interconnected by a lactam bond or a lactam-type bond or a lactone bond or a lactone-type bond or an amide bond or a hydrazone- and/or hydrazide-type bridge, or by being connected to one or more further structural unit(s) selected from amino acids and amino acid analogues and other units

whose molecular weight is no more than 270 and that are connected and interconnected by said types of bond(s) and/or bridges; forming a cyclic structure or cyclic structures in which the motif(s) Dd-Ee-Ff is/are the intermediary amino acid(s) and/or amino acid analogue(s) and/or are part(s) thereof, said cyclic structure(s) being defined by the the intermediary amino acids and other said constituents and bond(s) and/or bridge(s); and/or

wherein the motif Dd-Ee-Ff forms or each one of the motifs Dd-Ee-Ff forms or one or more of them each form(s) part of a structure comprising two units of amino acid(s) and/or amino acid analogue(s), that are spaced apart by a number of 3 to 20, preferably 3 to 9, more preferably 3 to 6, intermediary amino acid(s) and/or amino acid analogue(s) and interconnected by a lactam bond or a lactam-type bond or a lactone bond or a lactone-type bond or an amide bond or a hydrazone- and/or hydrazide-type bridge, or by being connected to one or more further structural unit(s) selected from amino acids and amino acid analogues that are connected and interconnected by said types of bond(s) and/or bridges, forming a cyclic structure or cyclic structures in which the motif(s) Dd-Ee-Ff is/are the intermediary amino acid(s) and/or amino acid analogue(s) and/or are part(s) thereof, said cyclic structure(s) being defined by the the intermediary amino acids and other said constituents and bond(s) and/or bridge(s).

70. The targeting unit according to claim 69, wherein the number of the intermediary amino acid(s) and/or amino acid analogue(s) is 3.

71. The targeting unit according to any one of claims 50 to 70,

that comprises one or more cyclic structure(s) that comprises or that each comprise or one or more of which each comprise(s) a bond between a unit or residue XX and a unit or residue YY, by virtue of which bond the structure(s) is/are cyclic, and that has been made or can be formally considered as having been made by reacting XX and YY; wherein

XX is selected from the group of: amino acid residues, amino acid analogue residues, other structural units and residues whose molecular weight is no more than 270, and

each XX comprises at least one amino group or substituted amino group or substituted or unsubstituted hydrazine, hydrazide or hydrazone moiety, or an activated and/or protected form of any of these, that can participate and is participating in an amide, peptide, hydrazide and/or hydrazone bond or bridge, and

YY is selected from the group of: amino acid residues, amino acid analogue residues, other structural units and residues whose molecular weight is no more than 270, and

each YY comprises at least one carboxyl, activated carboxyl, ester, activated ester, acyl halide, *N*-carboxanhydride, carboxylic acid anhydride and/or related functional group, or an activated and/or protected form of any of these, that can participate and is participating in an amide, peptide, hydrazide and/or hydrazone bond or bridge;

and/or

wherein, for each cyclic structure that has been made or can be formally considered as having been made by reacting XX and YY, independent of other cyclic structures if present,

XX comprises at least one amino group or substituted amino group or substituted or unsubstituted hydrazine, hydrazide or hydrazone moiety, or an activated and/or protected form of any of these, that is neither the alpha amino group nor an activated and/or protected form thereof; and/or

YY comprises at least one carboxyl, activated carboxyl, ester, activated ester, acyl halide, *N*-carboxanhydride, carboxylic acid anhydride and/or related functional group, or an activated and/or protected form of any of these, that is neither the *C*-terminal carboxyl group nor an activated and/or protected form thereof;

and/or

wherein the cyclic structure(s) or one or more of them is/are/has been/have been/was/were made by reacting XX and YY or can be formally considered to have been made by reaction of XX and YY, and for each such cyclic structure, independently of other cyclic structure(s) if present, either XX or YY or both have been orthogonally and/or pseudoorthogonally and/or quasiorthogonally and/or semiorthogonally protected, in addition to possible other type(s) of protection that may or may not have been used;

and/or

wherein in that one or more cyclic structure(s) have been made with the aid of two units selected from amino acids and amino acid analogues, one of which

carried an orthogonally or quasiorthogonally or pseudoorthogonally protected amino group or an orthogonally or quasiorthogonally or pseudoorthogonally protected substituted amino group or an orthogonally or quasiorthogonally or pseudoorthogonally protected hydrazide moiety or an orthogonally or quasiorthogonally or pseudoorthogonally protected substituted hydrazide moiety, and the other one of which carried an orthogonally or quasiorthogonally or pseudoorthogonally protected carboxyl group.

72. The targeting unit according to any one of claims 50 to 71, that comprises one or more motif(s) selected from the group of: IRE, IRD, LRE, LRD, ERI, DRI, ERL, DRL, RIE, REI, IER, EIR, RLE, REL, LER, ELR, DIR, IDR, RDI, RID, DLR, LDR, RDL and RLD and structural and/or functional analogues thereof; preferably from the group of: IRE, IRD, LRE, LRD, ERI, DRI, ERL and DRL and structural and/or functional analogues thereof; wherein the amino acid residues I, L, R, E and D each can optionally be, independently of the others, and in each case independently of other motif(s) if present, either in the L form or in the D form, and any other structural part(s)/unit(s) in the form of any optical isomer(s).

73. The targeting unit according to any one of claims 50 to 72, wherein

each motif Dd-Ee-Ff comprising amino acids comprises only L amino acids or D amino acids but not both, independently of the other motif(s) if present; and/or

each motif Dd-Ee-Ff comprising amino acids comprises only L amino acids; and/or

each motif Dd-Ee-Ff comprising amino acids comprises only D amino acids; and/or

at least one motif Dd-Ee-Ff and/or at least one targeting unit comprises one or more L amino acid(s) and at least one D amino acid; and/or

at least one motif Dd-Ee-Ff and/or targeting unit comprises at least one beta amino acid and/or other amino acid that is not an alpha amino acid, and/or at least one amino acid and/or amino acid analogue that comprise(s) one or more unnatural side chain(s).

74. The targeting unit according to any one of claims 50 to 73, wherein the motif(s) Dd-Ee-Ff or one or more of them is/are selected from those indicated in the Table in claim 24, and/or from peptidyl and/or peptidomimetic analogues of those specific motif sequences, and preferably from those indicated on rows 1-16 of the Table in claim 24, and/or from peptidyl and/or peptidomimetic analogues of the specific motif sequences

indicated on said rows, and more preferably from those indicated on rows 1-8 of the Table in claim 24, and/or from peptidyl and/or peptidomimetic analogues of the specific motif sequences indicated on said rows.

75. The targeting unit according to any one of claims 50 to 74, that comprises

one or more motif(s) selected from the group of: IRE, IRD, LRE, LRD, ERI, DRI, ERL, DRL, RIE, REI, IER, EIR, RLE, REL, LER, ELR, DIR, IDR, RDI, RID, DLR, LDR, RDL and RLD and structural and/or functional analogues thereof; and preferably selected from the group of: IRE, IRD, LRE, LRD, ERI, DRI, ERL, DRL and structural and/or functional analogues thereof; and also comprises at least two amino acid residues selected from the group of cysteine and homocysteine, and that there is for each motif at least one cysteine and/or homocysteine residue either directly bonded to the aminoterminal amino acid of the motif or separated from it in the aminoterminal direction by 1 to 8 intermediary amino acid residues; and wherein there is for each motif at least one cysteine and/or homocysteine residue either directly bonded to the carboxyterminal amino acid of the motif or separated from it in the carboxyterminal direction by 1 to 8 intermediary amino acid residues; and wherein optionally the amino acid residues I, L, R, E and D each can be, independently of the others, and in each case independently of other motif(s) if present, either in the L form or in the D form and any other structural part(s)/unit(s) in the form of any optical isomer(s), and wherein the cysteine and/or homocysteine residue(s) or some of them may or may not be in the oxidized (disulphide) form and the targeting unit(s) or one or more of them may or may not be cyclic.

76. The targeting unit according to any one of claims 50 to 75, wherein

the targeting unit is cyclic and/or comprises one or more cyclic structure(s); and/or
the targeting unit is cyclic so that the motif or motifs Dd-Ee-Ff or one or more of the motif(s) Dd-Ee-Ff is/are included in one or more cyclic structures; and/or

the targeting unit is cyclic so that one or more motif(s) Dd-Ee-Ff is/are included in one or more cyclic structure(s) and one or more motifs Dd-Ee-Ff are not included in a cyclic structure or cyclic structures; and/or

the targeting unit is not cyclic; and/or

the targeting unit is cyclic but no cyclic structure includes any disulphide bridge and/or one or more thiol groups are in the unoxidized -SH form; and/or

the targeting unit is cyclic so that the sole motif Dd-Ee-Ff or all of the motifs is/are included in one or more cyclic structures.

77. The targeting unit according to any one of claims 50 to 76, wherein each motif comprises

only L amino acids or D amino acids but not both, independently of the other motif(s) if present; and/or

only L amino acids; and/or

only D amino acids; and/or

at least one motif Dd-Ee-Ff and/or targeting unit comprises L amino acids and at least one D amino acid; and/or

at least one motif Dd-Ee-Ff and/or targeting unit comprises at least one beta amino acid and/or other amino acid that is not an alpha amino acid; and/or

at least one amino acid and/or amino acid analogue that comprise(s) one or more unnatural side chain(s).

78. The targeting unit according to any one of claims 50 to 77, that comprises one or more sequence(s) selected from the group of: CIREC, CIRDC, CLREC, CLRDC, CERIC, CDRIC, CERLC, CDRLC, CRIEC, CREIC, CIERC, CEIRC, CRLEC, CRELC, CLERC, CELRC, CDIRC, CIDRC, CRDIC, CRIDC, CDLRC, CLDRC, CRDLC and CRLDC and structural and/or functional analogues thereof; preferably from the group of: CIREC, CIRDC, CLREC, CLRDC, CERIC, CDRIC, CERLC and CDRLC and structural and/or functional analogues thereof; more preferably from the group of: CIREC, CIRDC, CLREC and CLRDC and structural and/or functional analogues thereof;

wherein optionally:

said sequence(s), and/or subsequence(s) thereof not comprising C, and/or one or more of them and/or the targeting unit may and/or may not be cyclic, said sequences/subsequences independently of each other, and/or the amount and/or location(s) of cyclic structure(s) may vary and/or change; and/or

each motif Dd-Ee-Ff that comprises amino acids comprises only L amino acids or only D amino acids, independent of other possible motif(s); and/or

each motif Dd-Ee-Ff that comprises amino acids comprises only L amino acids; and/or

each motif Dd-Ee-Ff that comprises amino acids comprises only D amino acids; and/or

at least one motif Dd-Ee-Ff and/or targeting unit comprises L amino acids and at least one D amino acid; and/or

at least one motif Dd-Ee-Ff and/or targeting unit comprises at least one beta amino acid and/or other amino acid that is not an alpha amino acid, and/or at least one amino acid and/or amino acid analogue that comprise(s) one or more unnatural side chain(s).

79. The targeting unit according to any one of claims 50 to 78, that is cyclic and/or comprises one or more cyclic structure(s) because of a disulphide bond between the cysteine residues in each or one or more or all subsequence(s) comprising a motif.

80. The targeting unit according to any one of claims 50 to 79, that comprises one or more sequence(s) CIREC and/or CERIC and/or one or more structural and/or functional analogue(s) thereof.

81. The targeting unit according to any one of claims 50 to 80, that comprises one or more motif(s) selected from the group of: IRE, IRD, LRE, LRD, ERI, DRI, ERL, DRL, RIE, REI, IER, EIR, RLE, REL, LER, ELR, DIR, IDR, RDI, RID, DLR, LDR, RDL and RLD and structural and/or functional analogue(s) thereof; preferably from the group of: IRE, IRD, LRE, LRD, ERI, DRI, ERL and DRL and structural and/or functional analogue(s) thereof; and that comprises one or more cyclic structure(s) so that said motif(s) or one or more of them is/are included in said cyclic structure or in one or more of said cyclic structure(s).

82. The targeting unit according to any one of claims 50 to 81, wherein

the cyclic structure or one or more of the cyclic structures comprise(s) one or more lactam structure(s) and/or one or more lactam-type structure(s) and/or one or more lactone structure(s) and/or one or more lactone-type structure(s) and/or one or more disulphide bridge(s); and/or

the cyclic structure or one or more of the cyclic structures comprise(s) one or more lactam structure(s) and/or one or more lactam-type structure(s) and/or one or more lactone structure(s) and/or one or more lactone-type structure(s); said structure or one or more of said structures being prepared with the aid of one or more amino acid(s) and/or amino acid analogue(s) and/or derivative(s) and/or protected and/or resin-bound and/or activated derivative(s) and/or analogue(s) thereof, that, in addition to the group(s) necessary and/or used for construction of a non-cyclic form or non-cyclic forms of the structure(s), comprise(s) one or more additional functional group(s) and/or their equivalent(s) that can be used for the synthesis/syntheses and/or spontaneous formation(s) of said cyclic structure(s) or one or more of them; and/or

the additional functional group(s) and/or their equivalent(s) that can be used for the synthesis/syntheses and/or spontaneous formation(s) of said cyclic structure(s) or one or more of them, or one or more of said additional functional group(s) and/or their equivalent(s), is/are selected from the group of: amino, substituted amino, carboxyl, hydroxyl, and any resin-bound and/or protected and/or activated form(s) and/or modification(s) of amino, substituted amino, carboxyl and/or hydroxyl; and/or

the cyclic structure or one or more of the cyclic structures comprise(s) one or more lactam structure(s) and/or one or more lactam-type structure(s); said structure or one or more of said structures being prepared with the aid of one or more amino acid(s) and/or amino acid analogue(s) and/or derivative(s) and/or protected and/or resin-bound and/or activated and/or related derivative(s) and/or analogue(s) thereof, that, in addition to the group(s) necessary and/or used for construction of a non-cyclic form or non-cyclic forms of the structure(s), comprise(s) one or more additional functional group(s) and/or their equivalent(s) that can be used for the synthesis/syntheses and/or spontaneous formation(s) of said cyclic structure(s) or one or more of them; and/or

the additional functional group(s) and/or their equivalent(s) that can be used for the synthesis/syntheses and/or spontaneous formation(s) of said cyclic structure(s) or one or more of them, or one or more of said additional functional group(s) and/or their equivalent(s), is/are selected from the group of: amino, substituted amino, carboxyl, and any resin-bound and/or protected and/or activated form(s) and/or modification(s) of amino, substituted amino and/or carboxyl; and/or

one or more orthogonally and/or quasiorthogonally and/or semiorthogonally and/or pseudoorthogonally protected amino acid(s) and/or amino acid analogue(s) and/or peptide(s) and/or peptide analogue(s), and/or one or more protected and/or activated and/or resin-bound and/or other bound and/or related form(s) of one or more of them, are used in

one or more step(s) of the formation of the cyclic structure(s) or one or more of the cyclic structures; and/or

one or more substance(s) and/or material(s) comprising one or more orthogonally and/or quasiorthogonally and/or semiorthogonally and/or pseudoorthogonally protected functional group(s) and/or their equivalent(s), is/are used, said protected functional group(s) and/or their equivalent(s) being selected from the group of: amino, substituted amino, and carboxyl;

the cyclic structure(s) or one or more of the cyclic structures is/are made by spontaneous and/or assisted and/or catalyzed reaction between group A and group B, or between the reaction of two or more groups A with an equal number of groups B, wherein group(s) A is/are selected from the group of carboxyl, activated carboxyl and acyl halide, and group B is selected from the group of amino, substituted amino, activated amino, activated substituted amino, hydrazine, hydrazone, hydrazide, substituted and/or activated hydrazine, substituted and/or activated hydrazone, substituted and/or activated hydrazide and hydroxyl; and/or

the cyclic structure(s) or one or more of the cyclic structures is/are made by spontaneous and/or assisted and/or catalyzed reaction between group A and group B, or between the reaction of two or more groups A with an equal number of groups B, wherein group A and/or group B, or one or more of groups A and/or of groups B, is/are liberated from one or more orthogonally and/or quasiorthogonally and/or semiorthogonally and/or pseudoorthogonally protected functional group(s) and/or their equivalent(s) and one or more of them is/are or is/are not activated.

83. The targeting unit according to any one of claims 50 to 82, that comprises

one or more sequence(s) LRELSMGYFK and/or IQLRDWGFIL and/or one or more structural and/or functional analogues thereof, wherein optionally each of the amino acids other than G may be in the L form or in the D form and any other structural part(s)/unit(s) in the form of any optical isomer(s), independently of other amino acids and/or other structural part(s)/unit(s); and/or

one or more motif(s) LRE and/or LRD and/or one or more structural and/or functional analogues thereof, and also comprise(s) one or more subsequence(s) GF and/or GY and/or GYF and/or GFY and/or one or more structural and/or functional analogue(s) thereof, and optionally also comprise(s) one or more of any of the amino acids I, Q, L, W, S, M, G, Y, F, K and/or of their structural and/or functional analogues, wherein optionally each of the

amino acids other than G may be in the L form or in the D form and any other structural part(s)/unit(s) in the form of any optical isomer(s), independently of other amino acids and/or other structural part(s)/unit(s).

84. The targeting unit according to any one of claims 50 to 83, wherein any cysteine and/or homocysteine residue(s) and/or other residue(s) and/or unit(s) comprising and/or potentially comprising -SH that are present in the unit are in the unoxidized -SH form and not in the oxidized -S-S- form; and/or at least one of the cysteine and/or homocysteine residue(s) and/or other residue(s) and/or unit(s) comprising and/or -SH and/or potentially comprising either -SH or -S-S-, that is/are present in the unit is in the unoxidized -SH form, being not in the oxidized -S-S- form; and/or any cysteine and/or homocysteine residue(s) and/or other residue(s) and/or unit(s) comprising -SH or -S-S- or potentially comprising -SH and/or -S-S-, that are present in the unit are in the oxidized -S-S- form and not in the unoxidized -SH form; and/or any cysteine and/or homocysteine residue(s) and/or other residue(s) and/or unit(s) comprising -SH and/or potentially comprising -SH or -S-S-, that are present in the targeting unit are in the oxidized -S-S- form and not in the unoxidized -SH form; or that in the case of an uneven number of -SH and -S-S- sulphurs altogether, any cysteine and/or homocysteine residue(s) and/or other residue(s) and/or unit(s) comprising -SH and/or potentially comprising -SH or -S-S-, except for one -S- (one -SH), that are present in the targeting unit are in the oxidized -S-S- form and not in the unoxidized -SH form, one -SH and only one being in the unoxidized (reduced) -SH form; and/or at least two cysteine and/or homocysteine residue(s) and/or other residue(s) and/or unit(s) comprising -SH or -S-S- or potentially comprising -SH and/or -S-S-, that are present in the targeting unit are in the oxidized -S-S- form and not in the unoxidized -SH form.

85. The targeting unit according to any one of claims 50 to 84, wherein the sequence(s) comprising the motif or motifs Dd-Ee-Ff or one or more of the motifs, and/or a subsequence/subsequences of one or more or each of said sequences or of the said sequence, is/are selected from the group of: CyIRECyy, CyIRDCyy, CyLRECyy, CyLRDCyy, CyERICyy, CyDRICyy, CyERLCyy, CyDRLCyy, CyRIECyy, CyREICyy, CyIERCyy, CyEIRCyy, CyRLECyy, CyRELCyy, CyLERCyy, CyELRCyy, CyDIRCyy, CyIDRCyy, CyRDICyy, CyRIDCyy, CyDLRCyy, CyLDRCyy, CyRDLCyy and CyRLDCyy and structural and/or functional analogues thereof;

wherein Cy in each case independently means: homocysteine or cysteine; or another amino acid or amino acid analogue, or another structure with a formula/molecular weight no more than 270, comprising a thiol group or potentially comprising a thiol group or an oxidized thiol group; or an amino acid or an amino acid analogue, or another structure with a formula/molecular

weight no more than 270, that is capable of forming a cyclic structure by reacting, as such and/or as activated and/or protected and/or deprotected, with Cyy,

and Cyy means, independently in each case and independently of Cy: homocysteine or cysteine; or another amino acid or amino acid analogue, or another structure with a formula/molecular weight no more than 270, comprising a thiol group or potentially comprising a thiol group or an oxidized thiol group; or an amino acid or an amino acid analogue, or another structure with a formula/molecular weight no more than 270, that is capable of forming a cyclic structure by reacting, as such or as activated and/or protected and/or deprotected, with Cy, the reaction giving rise to the formation of a lactam or lactone or hydrazone-type or other cyclic structure;

or Cy and Cyy together mean a structural part or moiety that makes the structure cyclic;

and wherein motif(s) comprising amino acid(s) may optionally comprise L amino acid(s) and/or D amino acid(s) and any other structural part(s)/unit(s) any optical isomer(s), and said sequence(s) and/or subsequence(s) and/or one or more of them and/or the targeting unit may and/or may not be cyclic, said sequences/subsequences independently of each other, and/or the amount and/or location(s) of cyclic structure(s) may vary and/or change.

86. The targeting unit according to any one of claims 50 to 85, wherein

the linker unit(s) bind(s) and/or connect(s) to each other one or more identical and/or similar and/or different targeting unit substructures/parts/moieties/motifs and/or one or more unit(s) selected from the group of:

- linker units,
- solubility modifier units,
- stabilizer units,
- charge modifier units,
- spacer units,
- lysis and/or reaction and/or reactivity modifier units,
- internalizing and/or internalization enhancer and/or membrane interaction units and/or other local route and/or local attachment/local binding and/or distribution affecting units,
- adsorption enhancer units, and
- other related units;

and/or

the solubility modifier unit(s) enhance(s), decrease(s) and/or otherwise modify/modifies the solubility of the of targeting unit and/or its hydrolysis product(s) and/or other products and/or part(s) of it/them; and/or

the stabilizer unit(s) stabilize(s) the structure of targeting unit and/or its hydrolysis product(s) and/or part(s) of it/them; and/or

the charge modifier unit(s) increase(s), decrease(s) and/or otherwise modify/modifies the electrical charge(s) of the targeting unit and/or its hydrolysis product(s) and/or part(s) of it/them and/or one or more starting material(s) of it; and/or

the spacer unit(s) increase(s) the distance between specific units in the targeting units and/or its hydrolysis product(s) and/or part(s) of it/them and/or parts of its starting materials, and/or release(s) or decrease(s) steric hindrance and/or structural strain; and/or

the lysis and/or reaction and/or reactivity modifier unit(s) make(s) possible, and/or enhance(s) and/or make(s) more rapid and/or prevent(s) and/or inhibit(s) and/or make(s) more slow and/or quantitatively and/or qualitatively modifies/modify and/or change(s), and/or modifies/modify the course and/or products of, and/or alter(s) the prerequisites and/or optimal conditions of, and/or redirect(s), one or more hydrolytic and/or other lytic reaction(s) and/or other decomposition process(es) and/or reaction(s) and/or their continuation process(es) and/ reaction(s) of the targeting unit and/or one or more starting material(s) and/or constituents thereof and/or one or more of their product(s) of hydrolysis and/or of other type(s) of lysis and/or of decomposition and/or of reaction(s); and/or

the lysis and/or reaction and/or reactivity modifier unit(s) increase(s) the susceptibility of the targeting unit to one or more type(s) of enzymatic and/or non-enzymatic reaction(s) and/or process(es); and/or

the spacer unit(s) increase(s) the distance between specific units in the targeting unit and/or its/their hydrolysis product(s) and/or part(s) of it/them and/or parts of its/their starting materials, and/or release(s) and/or decrease(s) steric hindrance and/or structural strain; and/or

the lysis and/or reaction and/or reactivity modifier unit(s) make(s) possible, and/or enhance(s) and/or make(s) more rapid and/or prevent(s) and/or inhibit(s) and/or make(s) more slow and/or quantitatively and/or qualitatively modifies/modify and/or change(s),

and/or modifies/modify the course and/or products of, and/or alter(s) the prerequisites and/or optimal conditions of, and/or redirect(s), one or more hydrolytic and/or other lytic reaction(s) and/or other decomposition process(es) and/or reaction(s) and/or their continuation process(es) and/or reaction(s) of the targeting unit and/or one or more starting material(s) and/or constituents thereof and/or one or more of its/their product(s) of hydrolysis and/or of other type(s) of lysis and/or of decomposition and/or of reaction(s); and/or

the lysis and/or reaction and/or reactivity modifier unit(s) increase(s) the susceptibility of the targeting unit to one or more type(s) of enzymatic and/or non-enzymatic reaction(s) and/or process(es); and/or

the internalizing unit(s) and/or internalization enhancer unit(s) and/or membrane interaction unit(s) and/or other local route and/or local attachment/local binding and/or distribution affecting unit(s) enhance(s) and/or make(s) more rapid and/or cause(s) and/or give(s) rise to and/or prevent(s) and/or inhibit(s) and/or affect(s) in one or more way(s) one or more process(es) that affect(s) and/or determine(s) and/or cause(s) and/or modifies/modify the route and/or fate and/or further localization in the vicinity of the targeted area of the targeting unit and/or product(s) of its hydrolysis and/or other lysis and/or decomposition and/or other reaction(s), and/or cause(s) the internalization of the targeting unit and/or the binding of it onto and/or into cell membranes after the targeting unit and/or targeting agent have reacted their target(s); and/or

the adsorption enhancer unit(s) is/are such that it/they is/are not hydrolyzed or otherwise lost after absorption; and/or

the adsorption enhancer unit(s) is/are such that it/they is/are hydrolyzed off and/or otherwise lost after absorption.

87. The targeting unit according to any one of claims 50 to 86, that comprises one or more boron atom(s) and/or that comprises isotope-enriched boron and/or that comprises one or more paramagnetic atom(s) and/or paramagnetic unit(s)/fragment(s) and/or radioactive atom(s) and/or carbon-13 atom(s) and/or enriched carbon-13.

88. A targeting motif c h a r a c t e r i z e d in that it is and/or comprises

Dd-Ee-Ff

and/or is and/or comprises one or more salt(s), ester(s), amide(s), hydrazide(s), *N*-

substituted amide(s), *N*-substituted hydrazide(s), hydroxamic acid -type derivative(s), *C*-terminally decarboxylated analogue(s), *N*-substituted derivative(s), and/or any related analogue(s) and/or derivative(s) of Dd-Ee-Ff, and/or is and/or comprises any combination(s) thereof,

wherein

Dd is either Aa or Bb or Cc or Aa′ or Bb′ or Cc′, and
Ee is either Aa or Bb or Cc or Aa′ or Bb′ or Cc′, and
Ff is either Aa or Bb or Cc or Aa′ or Bb′ or Cc′, and
Dd-Ee-Ff comprises Aa/Aa′and Bb/Bb′ and Cc/Cc′, and

wherein

Aa is the L- or D- form of isoleucine, leucine, *tert*-leucine or valine, or a structural and/or functional analogue thereof comprising in its side chain a branched, non-branched and/or alicyclic structure with at least two similar or different atoms selected from the group of carbon atoms, silicon atoms, halogen atoms bonded to one or more carbon(s), ether-oxygens and thioether-sulphurs;

Bb is the L- or D- form of arginine, homoarginine or canavanine, or a structural and/or functional analogue thereof comprising at least one guanyl and/or amidino group or a related group that has or can through protonation obtain a delocalized positive charge;

Cc is the L- or D- form of glutamic acid or aspartic acid, or a structural and/or functional analogue thereof, comprising in its side chain at least one carboxyl group or esterified carboxyl group;

Aa′ is a branched or non-branched or cyclic non-aromatic, lipophilic and/or hydrophobic amino acid or amino acid analogue or derivative or a structural and/or functional analogue thereof, or an amino acid or carboxylic acid or amino acid analogue or derivative or carboxylic acid analogue or derivative that has one or more lipophilic carborane-type and/or other lipophilic boron-containing side chain(s) or its/their equivalent(s) or another lipophilic cage-type structure;

Bb′ is an amino acid or amino acid analogue or derivative or a structural and/or functional analogue thereof, that comprises one or more guanyl

group(s) and/or amidino group(s) and/or its/their analogue(s) and/or derivative(s) and/or structural and/or functional equivalent(s) and/or one or more group(s) that comprise(s) at least two nitrogen atoms each and has/have or can gain a delocalized positive charge;

Cc′ is an amino acid or amino acid analogue or derivative or a structural and/or functional analogue thereof that comprises: one or more side-chain carboxyl group(s) and/or esterified carboxyl group(s), and/or ketoxime and/or aldoxime and/or hydroxamic acid group(s) and/or ketone- and/or aldehyde-carbonyl(s),

and/or Dd-Ee-Ff is and/or comprises a structural and/or functional analogue of a structure or structures Dd-Ee-Ff where Dd-Ee-Ff is as defined above, and/or comprises one or more salt(s), ester(s), amide(s), hydrazide(s), *N*-substituted amide(s), *N*-substituted hydrazide(s), hydroxamic acid -type derivative(s), *C*-terminally decarboxylated analogue(s), *N*-substituted derivative(s), and/or any related analogue(s) and/or derivative(s) thereof, and/or any combination(s) thereof.

89. The targeting motif according to claim 88, characterized in that it exhibits selective binding to one or more type(s) of: tumors and/or cancer(s) and/or tumor cells and/or cancer cells and/or malignant cells and/or transformed cells and/or tumor tissues and/or cancer tissues and/or malignant tissues and/or transformed tissues and/or leukemia cells and/or malignant blood cells and/or tranformed blood cells and/or related cells and/or tissues and/or tumor endothelium and/or activated endothelium and/or angiogenic endothelium and/or tumor-endothelium cells and/or activated-endothelium cells and/or angiogenic endothelium cells, and/or their like.

90. The targeting motif according to claim 88 or claim 89, characterized in that it exhibits selective binding to one or more type(s) of: tumors and/or cancer(s) and/or tumor cells and/or cancer cells and/or malignant cells and/or transformed cells and/or tumor tissues and/or cancer tissues and/or malignant tissues and/or transformed tissues and/or leukemia cells and/or malignant blood cells and/or tranformed blood cells and/or related cells and/or tissues and/or tumor endothelium and/or activated endothelium and/or angiogenic endothelium and/or tumor-endothelium cells and/or activated-endothelium cells and/or angiogenic endothelium cells, and/or their like, *in vivo* and/or *in vitro* and/or *ex vivo* and/or *in situ*.

91. The targeting motif according to any one of claims 88 to 90, characterized in that it exhibits selective binding to one or more type(s) of: tumors and/or cancer(s) and/or

tumor cells and/or cancer cells and/or malignant cells and/or transformed cells and/or tumor tissues and/or cancer tissues and/or malignant tissues and/or transformed tissues and/or leukemia cells and/or malignant blood cells and/or tranformed blood cells and/or related cells and/or tissues and/or tumor endothelium and/or activated endothelium and/or angiogenic endothelium and/or tumor-endothelium cells and/or activated-endothelium cells and/or angiogenic endothelium cells, and/or their like, *in vivo*.

92. The targeting motif according to any one of claims 88 to 91, characterized in that it exhibits selective binding to one or more type(s) of: tumors and/or cancer(s) and/or tumor cells and/or cancer cells and/or malignant cells and/or transformed cells and/or tumor tissues and/or cancer tissues and/or malignant tissues and/or transformed tissues and/or leukemia cells and/or malignant blood cells and/or tranformed blood cells and/or related cells and/or tissues and/or tumor endothelium and/or activated endothelium and/or angiogenic endothelium and/or tumor-endothelium cells and/or activated-endothelium cells and/or angiogenic endothelium cells, and/or their like, *in vitro* and/or *ex vivo*.

93. The targeting motif according to any one of claims 88 to 92, wherein the targeting unit(s) or one or more of them is/are capable of binding to one or more type(s) of: primary tumors and/or cancers, and/or tumor/cancer endothelium, and/or tumor/cancer metastases, and/or residive/residual tumors and/or cancers, and/or recurred/recurrent/relapsed tumors and/or cancers, and/or tumor cells; *in vivo* and/or *in vitro* and/or *ex vivo* and/or *in situ*.

94. The targeting motif according to any one of claims 88 to 93, wherein Dd-Ee-Ff is selected from the group of

Aa/Aa′- Bb/Bb′- Cc/Cc′,
Aa/Aa′- Cc/Cc′- Bb/Bb′,
Bb/Bb′- Aa/Aa′- Cc/Cc′,
Bb/Bb′- Cc/Cc′- Aa/Aa′,
Cc/Cc′- Aa/Aa′- Bb/Bb′ and
Cc/Cc′- Bb/Bb′- Aa/Aa′;

and/or comprises one or more structure(s) selected from said group and/or and/or is and/or comprises one or more salt(s), ester(s), amide(s), hydrazide(s), *N*-substituted amide(s), *N*-substituted hydrazide(s), hydroxamic acid -type derivative(s), *C*-terminally decarboxylated analogue(s), *N*-substituted derivative(s), and/or any related analogue(s) and/or derivative(s) thereof, and/or any combination(s) thereof.

95. The targeting motif according to any one of claims 88 to 94, wherein Dd-Ee-Ff is

selected from the group of

Aa/Aa′- Bb/Bb′- Cc/Cc′ and
Cc/Cc′- Bb/Bb′- Aa/Aa′;

and/or comprises one or more structure(s) selected from said group and/or and/or is and/or comprises one or more salt(s), ester(s), amide(s), hydrazide(s), *N*-substituted amide(s), *N*-substituted hydrazide(s), hydroxamic acid -type derivative(s), *C*-terminally decarboxylated analogue(s), *N*-substituted derivative(s), and/or any related analogue(s) and/or derivative(s) thereof, and/or any combination(s) thereof.

96. The targeting motif according to any one of claims 88 to 95, wherein Dd-Ee-Ff is and/or comprises

Aa/Aa′- Bb/Bb′- Cc/Cc′

and/or one or more salt(s), ester(s), amide(s), hydrazide(s), *N*-substituted amide(s), *N*-substituted hydrazide(s), hydroxamic acid -type derivative(s), *C*-terminally decarboxylated analogue(s), *N*-substituted derivative(s), and/or any related analogue(s) and/or derivative(s) thereof, and/or any combination(s) thereof.

97. The targeting motif according any one of claims 88 to 96, wherein Dd-Ee-Ff is selected from the group of

Aa-Bb-Cc,
Aa-Cc-Bb,
Bb-Aa-Cc,
Bb-Cc-Aa,
Cc-Aa-Bb and
Cc-Bb-Aa;

and/or comprises one or more structure(s) selected from said group and/or and/or is and/or comprises one or more salt(s), ester(s), amide(s), hydrazide(s), *N*-substituted amide(s), *N*-substituted hydrazide(s), hydroxamic acid -type derivative(s), *C*-terminally decarboxylated analogue(s), *N*-substituted derivative(s), and/or any related analogue(s) and/or derivative(s) thereof, and/or any combination(s) thereof.

98. The targeting motif according any one of claims 88 to 97, wherein Dd-Ee-Ff is selected from the group of

Aa-Bb-Cc and
Cc-Bb-Aa;

and/or comprises one or more structure(s) selected from said group and/or and/or is and/or comprises one or more salt(s), ester(s), amide(s), hydrazide(s), *N*-substituted amide(s), *N*-substituted hydrazide(s), hydroxamic acid -type derivative(s), *C*-terminally decarboxylated analogue(s), *N*-substituted derivative(s), and/or any related analogue(s) and/or derivative(s) thereof, and/or any combination(s) thereof.

99. The targeting motif according any one of claims 88 to 98, wherein Dd-Ee-Ff is and/or comprises

Aa-Bb-Cc

and/or one or more salt(s), ester(s), amide(s), hydrazide(s), *N*-substituted amide(s), *N*-substituted hydrazide(s), hydroxamic acid -type derivative(s), *C*-terminally decarboxylated analogue(s), *N*-substituted derivative(s), and/or any related analogue(s) and/or derivative(s) thereof, and/or any combination(s) thereof.

100. A targeting motif c h a r a c t e r i z e d in that it is and/or comprises

C-Dd-Ee-Ff-C

and/or is and/or comprises one or more salt(s), ester(s), amide(s), hydrazide(s), *N*-substituted amide(s), *N*-substituted hydrazide(s), hydroxamic acid -type derivative(s), *C*-terminally decarboxylated analogue(s), *N*-substituted derivative(s), and/or any related analogue(s) and/or derivative(s) of C-Dd-Ee-Ff-C, and/or is and/or comprises any combination(s) thereof,

wherein

Dd is either Aa or Bb or Cc or Aa′ or Bb′ or Cc′, and
Ee is either Aa or Bb or Cc or Aa′ or Bb′ or Cc′, and
Ff is either Aa or Bb or Cc or Aa′ or Bb′ or Cc′, and
Dd-Ee-Ff comprises Aa/Aa′and Bb/Bb′ and Cc/Cc′, and

wherein

Aa is the L- or D- form of isoleucine, leucine, *tert*-leucine or valine, or a

structural and/or functional analogue thereof comprising in its side chain a branched, non-branched and/or alicyclic structure with at least two similar or different atoms selected from the group of carbon atoms, silicon atoms, halogen atoms bonded to one or more carbon(s), ether-oxygens and thioether-sulphurs;

Bb is the L- or D- form of arginine, homoarginine or canavanine, or a structural and/or functional analogue thereof comprising at least one guanyl and/or amidino group or a related group that has or can through protonation obtain a delocalized positive charge;

Cc is the L- or D- form of glutamic acid or aspartic acid, or a structural and/or functional analogue thereof, comprising in its side chain at least one carboxyl group or esterified carboxyl group;

Aa′ is a branched or non-branched or cyclic non-aromatic, lipophilic and/or hydrophobic amino acid or amino acid analogue or derivative or a structural and/or functional analogue thereof, or an amino acid or carboxylic acid or amino acid analogue or derivative or carboxylic acid analogue or derivative that has one or more lipophilic carborane-type and/or other lipophilic boron-containing side chain(s) or its/their equivalent(s) or another lipophilic cage-type structure;

Bb′ is an amino acid or amino acid analogue or derivative or a structural and/or functional analogue thereof, that comprises one or more guanyl group(s) and/or amidino group(s) and/or its/their analogue(s) and/or derivative(s) and/or structural and/or functional equivalent(s) and/or one or more group(s) that comprise(s) at least two nitrogen atoms each and has/have or can gain a delocalized positive charge;

Cc′ is an amino acid or amino acid analogue or derivative or a structural and/or functional analogue thereof that comprises: one or more side-chain carboxyl group(s) and/or esterified carboxyl group(s), and/or ketoxime and/or aldoxime and/or hydroxamic acid group(s) and/or ketone- and/or aldehyde-carbonyl(s),

and/or Dd-Ee-Ff is a structural and/or functional analogue of a structure or structures where Dd-Ee-Ff is as defined above, or comprises one or more salt(s), ester(s), amide(s), hydrazide(s), *N*-substituted amide(s), *N*-substituted hydrazide(s), hydroxamic acid -type

derivative(s), *C*-terminally decarboxylated analogue(s), *N*-substituted derivative(s), and/or any related analogue(s) and/or derivative(s), and/or any combination(s) thereof;

and C is cysteine.

101. The targeting motif according to claim 100, characterized in that it exhibits selective binding to one or more type(s) of: tumors and/or cancer(s) and/or tumor cells and/or cancer cells and/or malignant cells and/or transformed cells and/or tumor tissues and/or cancer tissues and/or malignant tissues and/or transformed tissues and/or leukemia cells and/or malignant blood cells and/or tranformed blood cells and/or related cells and/or tissues and/or tumor endothelium and/or activated endothelium and/or angiogenic endothelium and/or tumor-endothelium cells and/or activated-endothelium cells and/or angiogenic endothelium cells, and/or their like.

102. The targeting motif according to claim 100 or claim 101, characterized in that:

it exhibits selective binding to one or more type(s) of: tumors and/or cancer(s) and/or tumor cells and/or cancer cells and/or malignant cells and/or transformed cells and/or tumor tissues and/or cancer tissues and/or malignant tissues and/or transformed tissues and/or leukemia cells and/or malignant blood cells and/or tranformed blood cells and/or related cells and/or tissues and/or tumor endothelium and/or activated endothelium and/or angiogenic endothelium and/or tumor-endothelium cells and/or activated-endothelium cells and/or angiogenic endothelium cells, and/or their like, *in vivo* and/or *in vitro* and/or *ex vivo* and/or *in situ*; and/or

it is capable of binding to one or more type(s) of: primary tumors and/or cancers, and/or tumor/cancer endothelium, and/or tumor/cancer metastases, and/or residive/residual tumors and/or cancers, and/or recurred/recurrent/relapsed tumors and/or cancers, and/or tumor cells; *in vivo* and/or *in vitro* and/or *ex vivo* and/or *in situ*.

103. The targeting motif according to any one of claims 88 to 102, characterized in that Dd-Ee-Ff is selected from the motif sequences Dd-Ee-Ff indicated in the Table in claim 24, and/or from peptidyl and/or peptidomimetic analogues of those specific motif sequences, prefereably from the motif sequences indicated on rows 1-16 of the Table and/or from peptidyl and/or peptidomimetic analogues of the specific motif sequences indicated on said rows, more preferably from the motif sequences indicated on rows 1-8 of the Table and/or from peptidyl and/or peptidomimetic analogues of the specific motif sequences indicated on said rows.

104. The targeting motif according to any one of claims 88 to 103, wherein Dd-Ee-Ff is selected from the group of: IRE, IRD, LRE, LRD, ERI, DRI, ERL, DRL, RIE, REI, IER, EIR, RLE, REL, LER, ELR, DIR, IDR, RDI, RID, DLR, LDR, RDL and RLD and structural and/or functional analogue(s) thereof, preferably from the group of: IRE, IRD, LRE, LRD, ERI, DRI, ERL and DRL and structural and/or functional analogue(s) thereof, more preferably from the group of: IRE, IRD, LRE and LRD.

105. The targeting motif according to any one of claims 88 to 104, characterized in that

it comprises a sequence selected from the group of: IRE, IRD, LRE, LRD, ERI, DRI, ERL, DRL, RIE, REI, IER, EIR, RLE, REL, LER, ELR, DIR, IDR, RDI, RID, DLR, LDR, RDL and RLD; prefereably from the group of: IRE, IRD, LRE, LRD, ERI, DRI, ERL and DRL; more preferably from the group of: IRE, IRD, LRE and LRD,

and that

it comprises also at least two amino acid residues selected from the group of: cysteine and homocysteine and other amino acids comprising a thiol group; preferably cysteine and homocysteine,

and that

there is at least one cysteine and/or homocysteine and/or other thiol-comprising amino acid residue, preferably cysteine and/or homocysteine residue, either directly bonded to the aminoterminal amino acid of the motif or separated from it in the aminoterminal direction by 1 to 8 intermediary amino acid residues, and that there is at least one cysteine and/or homocysteine residue either directly bonded to the carboxyterminal amino acid of the motif or separated from it in the carboxyterminal direction by 1 to 8 intermediary amino acid residues;

and that, optionally,

the cysteine and/or homocysteine and/or other thiol-comprising amino acid residues or one or some of them may or may not be in the oxidized (disulphide) form and the targeting motif may or may not be cyclic, and/or the amount of cyclic the structure(s) varies and/or may vary and/or changes and/or may change, and/or is and/or may be in a state of equilibrium and/or fluctuation and/or related phenomenon/phenomena, and/or is and/or may be uncertain and/or indifferent and/or undetermined, and/or wherein the degree of cyclicity is and/or may be partial and/or is and/or may be essentially total and/or is and/or may be essentially none and/or is and/or may be variant.

106. A targeting motif, characterized in that

it is selected from the group of: CIREC, CIRDC, CLREC, CLRDC, CERIC, CDRIC, CERLC, CDRLC, CRIEC, CREIC, CIERC, CEIRC, CRLEC, CRELC, CLERC, CELRC, CDIRC, CIDRC, CRDIC, CRIDC, CDLRC, CLDRC, CRDLC and CRLDC and structural and/or functional analogues thereof; preferably from the group of: CIREC, CIRDC, CLREC, CLRDC, CERIC, CDRIC, CERLC and CDRLC and structural and/or functional analogues thereof; more preferably from the group of: CIREC, CIRDC, CLREC and CLRDC and structural and/or functional analogues thereof;

and

it exhibits selective binding to one or more type(s) of: tumors and/or cancer(s) and/or tumor cells and/or cancer cells and/or malignant cells and/or transformed cells and/or tumor tissues and/or cancer tissues and/or malignant tissues and/or transformed tissues and/or leukemia cells and/or malignant blood cells and/or tranformed blood cells and/or related cells and/or tissues and/or tumor endothelium and/or activated endothelium and/or angiogenic endothelium and/or tumor-endothelium cells and/or activated-endothelium cells and/or angiogenic endothelium cells, and/or their like, *in vivo* and/or *in vitro* and/or *ex vivo* and/or *in situ*; and/or it is capable of binding to one or more type(s) of: primary tumors and/or cancers, and/or tumor/cancer endothelium, and/or tumor/cancer metastases, and/or residive/residual tumors and/or cancers, and/or recurred/recurrent/relapsed tumors and/or cancers, and/or tumor cells; *in vivo* and/or *in vitro* and/or *ex vivo* and/or *in situ*.

107. A targeting motif characterized in that

it is selected from the group of:

IQLRDWGFIL,
LRELSMGYFK,
subsequences of IQLRDWGFIL that comprise LRD,
subsequences of LRELSMGYFK that comprise LRE, and
structural and/or functional analogues thereof;

and

it exhibits selective binding to one or more type(s) of: tumors and/or cancer(s) and/or tumor cells and/or cancer cells and/or malignant cells and/or transformed cells and/or tumor tissues and/or cancer tissues and/or malignant tissues and/or transformed tissues and/or leukemia cells and/or malignant

blood cells and/or tranformed blood cells and/or related cells and/or tissues and/or tumor endothelium and/or activated endothelium and/or angiogenic endothelium and/or tumor-endothelium cells and/or activated-endothelium cells and/or angiogenic endothelium cells, and/or their like, *in vivo* and/or *in vitro* and/or *ex vivo* and/or *in situ*; and/or it is capable of binding to one or more type(s) of: primary tumors and/or cancers, and/or tumor/cancer endothelium, and/or tumor/cancer metastases, and/or residive/residual tumors and/or cancers, and/or recurred/recurrent/relapsed tumors and/or cancers, and/or tumor cells; *in vivo* and/or *in vitro* and/or *ex vivo* and/or *in situ*.

108. A targeting motif, characterized in that

it comprises LRE and/or LRD and/or a structural and/or functional analogue thereof, and

also comprises one or more subsequence(s) GF and/or GY and/or GYF and/or GFY and/or one or more structural and/or functional analogue(s) thereof, and

optionally also comprise(s) one or more of any of the amino acids I, Q, L, W and/or of their structural and/or functional analogues, and

it exhibits selective binding to one or more type(s) of: tumors and/or cancer(s) and/or tumor cells and/or cancer cells and/or malignant cells and/or transformed cells and/or tumor tissues and/or cancer tissues and/or malignant tissues and/or transformed tissues and/or leukemia cells and/or malignant blood cells and/or tranformed blood cells and/or related cells and/or tissues and/or tumor endothelium and/or activated endothelium and/or angiogenic endothelium and/or tumor-endothelium cells and/or activated-endothelium cells and/or angiogenic endothelium cells, and/or their like, *in vivo* and/or *in vitro* and/or *ex vivo* and/or *in situ*; and/or it is capable of binding to one or more type(s) of: primary tumors and/or cancers, and/or tumor/cancer endothelium, and/or tumor/cancer metastases, and/or residive/residual tumors and/or cancers, and/or recurred/recurrent/relapsed tumors and/or cancers, and/or tumor cells; *in vivo* and/or *in vitro* and/or *ex vivo* and/or *in situ*.

109. A targeting motif characterized in that

it comprises CyIRECyy, CyIRDCyy, CyLRECyy, CyLRDCyy, CyERICyy, CyDRICyy, CyERLCyy, CyDRLCyy, CyRIECyy, CyREICyy, CyIERCyy, CyEIRCyy, CyRLECyy,

CyRELCyy, CyLERCyy, CyELRCyy, CyDIRCyy, CyIDRCyy, CyRDICyy, CyRIDCyy, CyDLRCyy, CyLDRCyy, CyRDLCyy and/or CyRLDCyy and/or a structural and/or functional analogue of one or more of said sequences;

wherein:

Cy means homocysteine or cysteine; or another amino acid or amino acid analogue, or another structure with a formula/molecular weight no more than 270, comprising a thiol group or potentially comprising a thiol group or an oxidized thiol group; or an amino acid or an amino acid analogue, or another structure with a formula/molecular weight no more than 270, that is capable of forming a cyclic structure by reacting, as such and/or as activated and/or protected and/or deprotected, with Cyy,

and Cyy, independently of Cy, means homocysteine or cysteine; or another amino acid, or amino acid analogue, or another structure with a formula/molecular weight no more than 270, comprising a thiol group or potentially comprising a thiol group or an oxidized thiol group; or an amino acid or an amino acid analogue, or another structure with a formula/molecular weight no more than 270, that is capable of forming a cyclic structure by reacting, as such and/or as activated and/or protected and/or deprotected, with Cy, the reaction giving rise to the formation of a lactam or lactone or hydrazone-type or other cyclic structure;

and/or Cy and Cyy together mean a structural part or moiety that makes the motif cyclic and the total molecular/formula weight of Cy and Cyy altogether is no more than 540;

and it exhibits selective binding to one or more type(s) of: tumors and/or cancer(s) and/or tumor cells and/or cancer cells and/or malignant cells and/or transformed cells and/or tumor tissues and/or cancer tissues and/or malignant tissues and/or transformed tissues and/or leukemia cells and/or malignant blood cells and/or tranformed blood cells and/or related cells and/or tissues and/or tumor endothelium and/or activated endothelium and/or angiogenic endothelium and/or tumor-endothelium cells and/or activated-endothelium cells and/or angiogenic endothelium cells, and/or their like, *in vivo* and/or *in vitro* and/or *ex vivo* and/or *in situ*; and/or it is capable of binding to one or more type(s) of: primary tumors and/or cancers, and/or tumor/cancer endothelium, and/or tumor/cancer metastases, and/or residive/residual tumors and/or cancers, and/or recurred/recurrent/relapsed tumors and/or cancers, and/or tumor cells; *in vivo* and/or *in vitro* and/or *ex vivo* and/or *in situ*.

110. The targeting motif according to any one of claims 88 to 109, wherein

each one of the amino acid(s) and/or amino acid analogue(s) and/or other chiral unit(s)/part(s)/moiety/moieties can be, independently of the others, either in the L form or in the D form; and/or

the amino acid(s) and/or amino acid analogue(s) and/or other chiral unit(s)/part(s)/moiety/moieties independent of each other may be any stereoisomers; and/or

the amino acids comprise only L amino acids or D amino acids but not both; and/or

the amino acid(s) and/or amino acid analogue(s) and/or other chiral unit(s)/part(s)/moiety/moieties all comprise only L amino acids or D amino acids but not both;

and/or that comprises

only L amino acids and/or structural and/or functional analogues of L amino acids; and/or

only D amino acids and/or structural and/or functional analogues of D amino acids.

111. The targeting motif according any one of claims 88 to 110, wherein

the targeting motif is cyclic because of a disulphide bond and/or a lactam bond; and/or

the targeting motif is non-cyclic; and/or

the targeting motif is linear; and/or

the amount of cyclic structure(s) varies and/or may vary and/or changes and/or may change, and/or is and/or may be in a state of equilibrium and/or fluctuation and/or related phenomenon/phenomena, and/or is and/or may be uncertain and/or indifferent and/or undetermined, and/or wherein the degree of cyclicity is and/or may be partial and/or is and/or may be essentially total

and/or is and/or may be essentially none and/or is and/or may be variant.

112. The targeting motif according to any one of claims 88 to 111, that is included in one or more cyclic structure(s) and/or is cyclic in such a way that the structural moieties/units/residues Dd and Ee and Ff forming the motif Dd-Ee-Ff are included in the cyclic structure(s).

113. Peptides and peptidyl analogues and peptidomimetic analogues,

c h a r a c t e r i z e d in that they comprise one or more motif(s)

Dd-Ee-Ff

and/or one or more salt(s), ester(s), amide(s), hydrazide(s), *N*-substituted amide(s), *N*-substituted hydrazide(s), hydroxamic acid -type derivative(s), *C*-terminally decarboxylated analogue(s), *N*-substituted derivative(s), and/or any related analogue(s) and/or derivative(s), and/or their combination(s), of one or more such motif(s),

wherein

Dd is either Aa or Bb or Cc or Aa′ or Bb′ or Cc′, and
Ee is either Aa or Bb or Cc or Aa′ or Bb′ or Cc′, and
Ff is either Aa or Bb or Cc or Aa′ or Bb′ or Cc′, and
Dd-Ee-Ff comprises Aa/Aa′and Bb/Bb′ and Cc/Cc′, and

wherein

Aa is the L- or D- form of isoleucine, leucine, *tert*-leucine or valine, or a structural and/or functional analogue thereof comprising in its side chain a branched, non-branched and/or alicyclic structure with at least two similar or different atoms selected from the group of carbon atoms, silicon atoms, halogen atoms bonded to one or more carbon(s), ether-oxygens and thioether-sulphurs;

Bb is the L- or D- form of arginine, homoarginine or canavanine, or a structural and/or functional analogue thereof comprising at least one guanyl and/or amidino group or a related group that has or can through protonation obtain a delocalized positive charge;

Cc is the L- or D- form of glutamic acid or aspartic acid, or a structural and/or

functional analogue thereof, comprising in its side chain at least one carboxyl group or esterified carboxyl group;

Aa′ is a branched or non-branched or cyclic non-aromatic, lipophilic and/or hydrophobic amino acid or amino acid analogue or derivative or a structural and/or functional analogue thereof, or an amino acid or carboxylic acid or amino acid analogue or derivative or carboxylic acid analogue or derivative that has one or more lipophilic carborane-type and/or other lipophilic boron-containing side chain(s) or its/their equivalent(s) or another lipophilic cage-type structure;

Bb′ is an amino acid or amino acid analogue or derivative or a structural and/or functional analogue thereof, that comprises one or more guanyl group(s) and/or amidino group(s) and/or its/their analogue(s) and/or derivative(s) and/or structural and/or functional equivalent(s) and/or one or more group(s) that comprise(s) at least two nitrogen atoms each and has/have or can gain a delocalized positive charge;

Cc′ is an amino acid or amino acid analogue or derivative or a structural and/or functional analogue thereof that comprises: one or more side-chain carboxyl group(s) and/or esterified carboxyl group(s), and/or ketoxime and/or aldoxime and/or hydroxamic acid group(s) and/or ketone- and/or aldehyde-carbonyl(s),

and/or the motif(s) Dd-Ee-Ff or one or more of them is/are structural and/or functional analogue(s) of a structure or structures where Dd-Ee-Ff is as defined above;

and the molecular/formula weight of each of the peptides and peptidyl analogues and peptidomimetic analogues, as calculated without any counterions and/or their like, is no more than 400.

114. Peptides and peptidyl analogues and peptidomimetic analogues as defined in the characterizing part of claim 113, with the exception of the definition of the molecular/formula weight; wherein the molecular/formula weight of each of the peptides and peptidyl analogues and peptidomimetic analogues, as calculated without any counterions and/or their like, ranges from 350 to 550.

115. Peptides and peptidyl analogues and peptidomimetic analogues as defined in the characterizing part of claim 113, with the exception of the definition of the

molecular/formula weight; wherein the molecular/formula weight of each of the peptides and peptidyl analogues and peptidomimetic analogues, as calculated without any counterions and/or their like, ranges from 540 to 740.

116. Peptides and peptidyl analogues and peptidomimetic analogues as defined in the characterizing part of claim 113, with the exception of the definition of the molecular/formula weight; wherein the molecular/formula weight of each of the peptides and peptidyl analogues and peptidomimetic analogues, as calculated without any counterions and/or their like, ranges from 730 to 900.

117. Peptides and peptidyl analogues and peptidomimetic analogues as defined in the characterizing part of claim 113, with the exception of the definition of the molecular/formula weight; wherein the molecular/formula weight of each of the peptides and peptidyl analogues and peptidomimetic analogues, as calculated without any counterions and/or their like, ranges from 880 to 1100.

118. Peptides and peptidyl analogues and peptidomimetic analogues as defined in the characterizing part of claim 113, with the exception of the definition of the molecular/formula weight; wherein the molecular/formula weight of each of the peptides and peptidyl analogues and peptidomimetic analogues, as calculated without any counterions and/or their like, ranges from 1050 to 1500, preferably from 1050 to 1250.

119. Peptides and peptidyl analogues and peptidomimetic analogues as defined in the characterizing part of claim 113, with the exception of the definition of the molecular/formula weight; wherein the molecular/formula weight of each of the peptides and peptidyl analogues and peptidomimetic analogues, as calculated without any counterions and/or their like, ranges from 1450 to 2000, preferably from 1450 to 1750.

120. Peptides and peptidyl analogues and peptidomimetic analogues as defined in the characterizing part of claim 113, with the exception of the definition of the molecular/formula weight; wherein the molecular/formula weight of each of the peptides and peptidyl analogues and peptidomimetic analogues, as calculated without any counterions and/or their like, ranges from 1950 to 3500, preferably from 2000 to 2750.

121. Peptides according to any one of claims 113 to 120, that

comprise only natural and/or unnatural amino acid(s) and/or imino acid(s) and/or decarboxylated and/or amide and/or hydrazide and/or ester derivatives and/or analogues thereof, and optionally for cyclization purpose also one or more amino acid analogue(s)

and/or other moieties with a molecular weight of no more than 270 each, and may also comprise counterions and/or their like;

and/or

comprise only natural and/or unnatural amino acid(s) and/or imino acid(s) and/or decarboxylated and/or amide and/or hydrazide and/or ester derivatives and/or analogues thereof, and optionally also counterions and/or their like.

122. Any salt(s), ester(s), amide(s), hydrazide(s), *N*-substituted amide(s), any *N*-substituted hydrazide(s), hydroxamic acid derivative(s), decarboxylated analogue(s), *N*-substituted derivative(s), and any other related derivative(s) and/or analogue(s), protected derivative(s) and analogue(s), activated derivative(s) and analogue(s), resin-bound derivative(s) and analogue(s), and any combination(s) of any of such salt, derivative and/or analogue type(s) of any of the peptides and/or peptidyl analogues and/or peptidomimetic analogues as defined in any of claims 113 to 121.

123. Compounds that have the structural formula

Cy-Dd-Ee-Ff-Cyy

wherein Cy in each case independently means: homocysteine or cysteine; or another amino acid or amino acid analogue, or another structure with a formula/molecular weight no more than 270, comprising a thiol group or potentially comprising a thiol group or an oxidized thiol group; or an amino acid or an amino acid analogue, or another structure with a formula/molecular weight no more than 270, that is capable of forming a cyclic structure by reacting, as such and/or as activated and/or protected and/or deprotected, with Cyy,

and Cyy means, independently in each case and independently of Cy: homocysteine or cysteine; or another amino acid or amino acid analogue, or another structure with a formula/molecular weight no more than 270, comprising a thiol group or potentially comprising a thiol group or an oxidized thiol group; or an amino acid or an amino acid analogue, or another structure with a formula/molecular weight no more than 270, that is capable of forming a cyclic structure by reacting, as such or as activated and/or protected and/or deprotected, with Cy, the reaction giving rise to the formation of a lactam or lactone or hydrazone-type or other cyclic structure;

and/or Cy and Cyy together mean a structural part or moiety that makes the structure cyclic, and the formula weight of Cy-Cyy is no more than 540;

and wherein the motif(s) Dd-Ee-Ff is/are as defined in claim 1 and/or in claim 52 and/or in any other one(s) of the previous claims;

and wherein any amino acid(s) may comprise L amino acid(s) and/or D amino acid(s) and/or any other optical isomer(s);

and wherein the compounds Cy-Dd-Ee-Ff-Cyy may and/or may not be cyclic, and/or the amount and/or location(s) of cyclic structure(s) may vary and/or change;

and:

- any salt(s)
- any ester(s)
- any amide(s)
- any hydrazide(s)
- any *N*-substituted amide(s)
- any *N*-substituted hydrazide(s)
- any hydroxamic acid derivative(s)
- any decarboxylated analogue(s)
- any *N*-substituted derivative(s)
- any other related derivative(s)
- any other related analogue(s)
- any protected derivative(s) and analogue(s)
- any activated derivative(s) and analogue(s)
- any resin-bound derivative(s) and analogue(s)
- any combination(s) of any of such salt, derivative and/or analogue types

of any of the compounds as defined above.

124. Compounds that have the structural formula

$$Cy\text{-}Rr^{1}\text{-}Rr^{2}\text{-}...\text{-}Rr^{n}\text{-}Cyy$$

wherein Cy in each case independently means: homocysteine or cysteine; or another amino acid or amino acid analogue, or another structure with a formula/molecular weight no more than 270, comprising a thiol group or potentially comprising a thiol group or an oxidized thiol group; or an amino acid or an amino acid analogue, or another structure with a formula/molecular weight no more than 270, that is capable of forming a cyclic structure by reacting, as such and/or as activated and/or protected and/or deprotected, with Cyy,

and Cyy means, independently in each case and independently of Cy: homocysteine or cysteine; or another amino acid or amino acid analogue, or another structure with a formula/molecular weight no more than 270, comprising a thiol group or potentially comprising a thiol group or an oxidized thiol group; or an amino acid or an amino acid analogue, or another structure with a formula/molecular weight no more than 270, that is capable of forming a cyclic structure by reacting, as such or as activated and/or protected and/or deprotected, with Cy, the reaction giving rise to the formation of a lactam or lactone or hydrazone-type or other cyclic structure;

and/or Cy and Cyy together mean a structural part or moiety that makes the structure cyclic, and the formula weight of Cy-Cyy is no more than 540;

and wherein Rr^1 and Rr^2 and Rr^3 and so on and Rr^n each are, independently of each other, selected from the group of any optical and geometrical isomers of any natural and unnatural alpha-, beta-, gamma-, delta-, epsilon-, zeta-, eta-, theta-, kappa-, lambda-, mu-, nu-, xi-, omicron-, pi- and rho- and omega- amino acids/amino acid residues/amino acid units which amino acids/amino acid residues/amino acid units each comprise maximally 40 non-hydrogen atoms and an unlimited number of hydrogen atoms;

and wherein the structural fragment Rr^1-Rr^2-...-Rr^n comprises one or more motif(s) Dd-Ee-Ff and wherein the motif(s) Dd-Ee-Ff is/are as defined in claim 1 and/or in claim 52 and/or in any other one(s) of the previous claims;

and wherein the structural fragment Rr^1-Rr^2-...-Rr^n comprises 3 to 25, preferably 3 to 9, more preferably 3 to 6, and most preferably 3 amino acids/amino acid residues/amino acid units;

and wherein any amino acid(s)/amino acid residue(s)/amino acid unit(s) may comprise L amino acid(s) and/or D amino acid(s) and/or any other optical isomer(s);

and wherein the compounds Cy-Rr^1-Rr^2-...-Rr^n-Cyy may and/or may not be cyclic, and/or the amount and/or location(s) of cyclic structure(s) may vary and/or change;

and:

- any salt(s)
- any ester(s)
- any amide(s)
- any hydrazide(s)

- any *N*-substituted amide(s)
- any *N*-substituted hydrazide(s)
- any hydroxamic acid derivative(s)
- any decarboxylated analogue(s)
- any *N*-substituted derivative(s)
- any other related derivative(s)
- any other related analogue(s)
- any protected derivative(s) and analogue(s)
- any activated derivative(s) and analogue(s)
- any resin-bound derivative(s) and analogue(s)
- any combination(s) of any of such salt, derivative and/or analogue types

of the compounds as defined above.

125. Compounds that have the structural formula

Cy-Dd-Ee-Ff-Cyy

wherein:

Cy and Cyy, independently of each other, each mean:
homocysteine,
or cysteine,
or a natural or unnatural alpha-amino acid with a formula/molecular weight no more than 270, comprising a thiol group or potentially comprising a thiol group or an oxidized thiol group,

and a disulphide bridge may and/or may not exist between a thiol group of Cy and a thiol group of Cyy,

or wherein:

Cy means a natural or unnatural amino acid with a formula/molecular weight no more than 270, that comprises at least one amino group in addition to the alpha-amino group,

and Cyy means a natural or unnatural amino acid with a formula/molecular weight no more than 270, that comprises at least one carboxyl group in addition to the *C*-terminal carboxyl group,

and a lactam bond/bridge may and/or may not exist between an amino group of Cy and a carboxyl group of Cyy,

or wherein:

Cyy means a natural or unnatural amino acid with a formula/molecular weight no more than 270, that comprises at least one amino group in addition to the alpha-amino group,

and Cy means a natural or unnatural amino acid with a formula/molecular weight no more than 270, that comprises at least one carboxyl group in addition to the *C*-terminal carboxyl group,

and a lactam bond/bridge may and/or may not exist between an amino group of Cyy and a carboxyl group of Cy;

and wherein the motif(s) Dd-Ee-Ff is/are as defined in claim 1 and/or in claim 52 and/or in any other one(s) of the previous claims;

and wherein any amino acid(s) may comprise L amino acid(s) and/or D amino acid(s) and/or any other optical isomer(s);

and wherein the compounds Cy-Dd-Ee-Ff-Cyy may and/or may not be cyclic, and/or the amount and/or location(s) of cyclic structure(s) may vary and/or change;

and:

- any salt(s)
- any ester(s)
- any amide(s)
- any hydrazide(s)
- any *N*-substituted amide(s)
- any *N*-substituted hydrazide(s)
- any hydroxamic acid derivative(s)
- any decarboxylated analogue(s)
- any *N*-substituted derivative(s)
- any other related derivative(s)
- any other related analogue(s)
- any protected derivative(s) and analogue(s)
- any activated derivative(s) and analogue(s)

- any resin-bound derivative(s) and analogue(s)
- any combination(s) of any of such salt, derivative and/or analogue types

of any of the compounds as defined above.

126. Compounds that have the structural formula

$$Cy\text{-}Rr^{1}\text{-}Rr^{2}\text{-}...\text{-}Rr^{n}\text{-}Cyy$$

wherein:

Cy and Cyy, independently of each other, each mean:

homocysteine,
or cysteine,
or a natural or unnatural alpha-amino acid with a formula/molecular weight no more than 270, comprising a thiol group or potentially comprising a thiol group or an oxidized thiol group,

and a disulphide bridge may and/or may not exist between a thiol group of Cy and a thiol group of Cyy,

or wherein:

Cy means a natural or unnatural amino acid with a formula/molecular weight no more than 270, that comprises at least one amino group in addition to the alpha-amino group,

and Cyy means a natural or unnatural amino acid with a formula/molecular weight no more than 270, that comprises at least one carboxyl group in addition to the *C*-terminal carboxyl group,

and a lactam bond/bridge may and/or may not exist between an amino group of Cy and a carboxyl group of Cyy,

or wherein:

Cyy means a natural or unnatural amino acid with a formula/molecular weight no more than 270, that comprises at least one amino group in addition to the alpha-amino group,

and Cy means a natural or unnatural amino acid with a formula/molecular weight no more than 270, that comprises at least one carboxyl group in

addition to the *C*-terminal carboxyl group,

and a lactam bond/bridge may and/or may not exist between an amino group of Cyy and a carboxyl group of Cy;

and wherein Rr^1 and Rr^2 and Rr^3 and so on and Rr^n each are, independently of each other, selected from the group of any optical and geometrical isomers of any natural and unnatural alpha-, beta-, gamma-, delta-, epsilon-, zeta-, eta-, theta-, kappa-, lambda-, mu-, nu-, xi-, omicron-, pi- and rho- and omega- amino acids/amino acid residues/amino acid units which amino acids/amino acid residues/amino acid units each comprise maximally 40 non-hydrogen atoms and an unlimited number of hydrogen atoms;

and wherein the structural fragment Rr^1-Rr^2-...-Rr^n comprises one or more motif(s) Dd-Ee-Ff and wherein the motif(s) Dd-Ee-Ff is/are as defined in claim 1 and/or in claim 52 and/or in any other one(s) of the previous claims;

and wherein the structural fragment Rr^1-Rr^2-...-Rr^n comprises 3 to 25, preferably 3 to 9, more preferably 3 to 6, and most preferably 3 amino acids/amino acid residues/amino acid units;

and wherein any amino acid(s)/amino acid residue(s)/amino acid unit(s) may comprise L amino acid(s) and/or D amino acid(s) and/or any other optical isomer(s);

and wherein the compounds Cy-Rr^1-Rr^2-...-Rr^n-Cyy may and/or may not be cyclic, and/or the amount and/or location(s) of cyclic structure(s) may vary and/or change;

and:

- any salt(s)
- any ester(s)
- any amide(s)
- any hydrazide(s)
- any *N*-substituted amide(s)
- any *N*-substituted hydrazide(s)
- any hydroxamic acid derivative(s)
- any decarboxylated analogue(s)
- any *N*-substituted derivative(s)
- any other related derivative(s)
- any other related analogue(s)
- any protected derivative(s) and analogue(s)

- any activated derivative(s) and analogue(s)
- any resin-bound derivative(s) and analogue(s)
- any combination(s) of any of such salt, derivative and/or analogue types

of any of the compounds as defined above.

127. Compounds according to any one of claims 123 to 126, wherein the motif(s) Dd-Ee-Ff is/are selected from the group of: IRE, IRD, LRE, LRD, ERI, DRI, ERL, DRL, RIE, REI, IER, EIR, RLE, REL, LER, ELR, DIR, IDR, RDI, RID, DLR, LDR, RDL and RLD; preferably from the group of: IRE, IRD, LRE, LRD, ERI, DRI, ERL and DRL; more preferably from the group of: IRE, IRD, LRE and LRD;

and:

- any salt(s)
- any ester(s)
- any amide(s)
- any hydrazide(s)
- any *N*-substituted amide(s)
- any *N*-substituted hydrazide(s)
- any hydroxamic acid derivative(s)
- any decarboxylated analogue(s)
- any *N*-substituted derivative(s)
- any other related derivative(s)
- any other related analogue(s)
- any protected derivative(s) and analogue(s)
- any activated derivative(s) and analogue(s)
- any resin-bound derivative(s) and analogue(s)
- any combination(s) of any of such salt, derivative and/or analogue types

of any of the compounds as defined above.

128. Compounds according to any one of claims 123 to 127, wherein Cy and Cyy are, independently of each other, selected from the group of: cysteine and homocysteine, and their homologs comprising no more than 12 carbon atoms each; preferably from the group of cysteine and homocysteine;

and:

- any salt(s)
- any ester(s)

- any amide(s)
- any hydrazide(s)
- any *N*-substituted amide(s)
- any *N*-substituted hydrazide(s)
- any hydroxamic acid derivative(s)
- any decarboxylated analogue(s)
- any *N*-substituted derivative(s)
- any other related derivative(s)
- any other related analogue(s)
- any protected derivative(s) and analogue(s)
- any activated derivative(s) and analogue(s)
- any resin-bound derivative(s) and analogue(s)
- any combination(s) of any of such salt, derivative and/or analogue types

of any of the compounds as defined above.

129. Compounds according to any one of claims 123 to 128, wherein

Cy is selected from the group of: D and E, and their homologs comprising no more than 12 carbon atoms each, preferably from the group of D and E; and Cyy is selected from the group of: lysine and ornithine, and their homologs comprising no more than 12 carbon atoms each, preferably from the group of lysine and ornithine;

or wherein

Cyy is selected from the group of: D and E, and their homologs comprising no more than 12 carbon atoms each, preferably from the group of D and E; and Cy is selected from the group of: lysine and ornithine, and their homologs comprising no more than 12 carbon atoms each, preferably from the group of lysine and ornithine;

and:

- any salt(s)
- any ester(s)
- any amide(s)
- any hydrazide(s)
- any *N*-substituted amide(s)
- any *N*-substituted hydrazide(s)

- any hydroxamic acid derivative(s)
- any decarboxylated analogue(s)
- any *N*-substituted derivative(s)
- any other related derivative(s)
- any other related analogue(s)
- any protected derivative(s) and analogue(s)
- any activated derivative(s) and analogue(s)
- any resin-bound derivative(s) and analogue(s)
- any combination(s) of any of such salt, derivative and/or analogue types

of any of the compounds as defined above.

130. Compounds according to any one of claims 123 to 129, wherein:

the motif(s) Dd-Ee-Ff is/are selected from the group of: IRE, IRD, LRE, LRD, ERI, DRI, ERL, DRL, RIE, REI, IER, EIR, RLE, REL, LER, ELR, DIR, IDR, RDI, RID, DLR, LDR, RDL and RLD; preferably from the group of: IRE, IRD, LRE, LRD, ERI, DRI, ERL and DRL; more preferably from the group of: IRE, IRD, LRE and LRD;

and wherein Cy and Cyy are, independently of each other, selected from the group of: cysteine and homocysteine, and their homologs comprising no more than 12 carbon atoms each; preferably from the group of cysteine and homocysteine;

and wherein optionally:

a disulphide bridge exists between the thiol groups of Cy and Cyy, and/or

a disulphide bridge does not exist between the thiol groups of Cy and Cyy, and/or

the presence/number of disulphide bridge(s) is undetermined and/or uncertain and/or fluctuating and/or variable and/or subject to change and/or fluctuation;

and:

- any salt(s)
- any ester(s)
- any amide(s)
- any hydrazide(s)
- any *N*-substituted amide(s)

- any *N*-substituted hydrazide(s)
- any hydroxamic acid derivative(s)
- any decarboxylated analogue(s)
- any *N*-substituted derivative(s)
- any other related derivative(s)
- any other related analogue(s)
- any protected derivative(s) and analogue(s)
- any activated derivative(s) and analogue(s)
- any resin-bound derivative(s) and analogue(s)
- any combination(s) of any of such salt, derivative and/or analogue types

of any of the compounds as defined above.

131. Compounds according to any one of claims 123 to 130 wherein:

the motif(s) Dd-Ee-Ff is/are selected from the group of: IRE, IRD, LRE, LRD, ERI, DRI, ERL, DRL, RIE, REI, IER, EIR, RLE, REL, LER, ELR, DIR, IDR, RDI, RID, DLR, LDR, RDL and RLD; preferably from the group of: IRE, IRD, LRE, LRD, ERI, DRI, ERL and DRL; more preferably from the group of: IRE, IRD, LRE and LRD;

and wherein:

Cy is selected from the group of: D and E, and their homologs comprising no more than 12 carbon atoms each, preferably from the group of D and E; and Cyy is selected from the group of: lysine and ornithine, and their homologs comprising no more than 12 carbon atoms each, preferably from the group of lysine and ornithine; or

Cyy is selected from the group of: D and E, and their homologs comprising no more than 12 carbon atoms each, preferably from the group of D and E; and Cy is selected from the group of: lysine and ornithine, and their homologs comprising no more than 12 carbon atoms each, preferably from the group of lysine and ornithine;

and wherein optionally:

a lactam bridge exists between Cy and Cyy, or
a lactam bridge does not exist between Cy and Cyy, or
the presence/number of lactam bridge(s) is undetermined and/or uncertain

and/or fluctuating and/or variable and/or subject to change and/or fluctuation;

and:

- any salt(s)
- any ester(s)
- any amide(s)
- any hydrazide(s)
- any *N*-substituted amide(s)
- any *N*-substituted hydrazide(s)
- any hydroxamic acid derivative(s)
- any decarboxylated analogue(s)
- any *N*-substituted derivative(s)
- any other related derivative(s)
- any other related analogue(s)
- any protected derivative(s) and analogue(s)
- any activated derivative(s) and analogue(s)
- any resin-bound derivative(s) and analogue(s)
- any combination(s) of any of such salt, derivative and/or analogue types

of any of the compounds as defined above.

132. The compounds:
CIREC, CIRDC, CLREC, CLRDC, CERIC, CDRIC, CERLC, CDRLC, CRIEC, CREIC, CIERC, CEIRC, CRLEC, CRELC, CLERC, CELRC, CDIRC, CIDRC, CRDIC, CRIDC, CDLRC, CLDRC, CRDLC and CRLDC;

in which optionally:

a disulphide bridge exists between the thiol groups, and/or
a disulphide bridge does not exist between the thiol groups, and/or
the presence/number of disulphide bridge(s) is undetermined and/or uncertain and/or fluctuating and/or variable and/or subject to change and/or fluctuation and/or uncomplete and/or partial;

and:

- any salt(s)
- any ester(s)
- any amide(s)
- any hydrazide(s)

- any *N*-substituted amide(s)
- any *N*-substituted hydrazide(s)
- any hydroxamic acid derivative(s)
- any decarboxylated analogue(s)
- any *N*-substituted derivative(s)
- any other related derivative(s)
- any other related analogue(s)
- any protected derivative(s) and analogue(s)
- any activated derivative(s) and analogue(s)
- any resin-bound derivative(s) and analogue(s)
- any combination(s) of any of such salt, derivative and/or analogue types

of any of said compounds.

133. The compounds:
CIREC, CIRDC, CLREC, CLRDC;

in which optionally:

a disulphide bridge exists between the thiol groups, and/or
a disulphide bridge does not exist between the thiol groups, and/or
the presence/number of disulphide bridge(s) is undetermined and/or uncertain and/or fluctuating and/or variable and/or subject to change and/or fluctuation and/or uncomplete and/or partial;

and:

- any salt(s)
- any ester(s)
- any amide(s)
- any hydrazide(s)
- any *N*-substituted amide(s)
- any *N*-substituted hydrazide(s)
- any hydroxamic acid derivative(s)
- any decarboxylated analogue(s)
- any *N*-substituted derivative(s)
- any other related derivative(s)
- any other related analogue(s)
- any protected derivative(s) and analogue(s)
- any activated derivative(s) and analogue(s)

- any resin-bound derivative(s) and analogue(s)
- any combination(s) of any of such salt, derivative and/or analogue types

of any of said compounds.

134. The compounds:

CERIC, CDRIC, CERLC, CDRLC, CRIEC, CREIC, CIERC, CEIRC, CRLEC, CRELC, CLERC, CELRC, CDIRC, CIDRC, CRDIC, CRIDC, CDLRC, CLDRC, CRDLC and CRLDC;

in which optionally:

a disulphide bridge exists between the thiol groups, and/or
a disulphide bridge does not exist between the thiol groups, and/or
the presence/number of disulphide bridge(s) is undetermined and/or uncertain and/or fluctuating and/or variable and/or subject to change and/or fluctuation and/or uncomplete and/or partial;

and:

- any salt(s)
- any ester(s)
- any amide(s)
- any hydrazide(s)
- any *N*-substituted amide(s)
- any *N*-substituted hydrazide(s)
- any hydroxamic acid derivative(s)
- any decarboxylated analogue(s)
- any *N*-substituted derivative(s)
- any other related derivative(s)
- any other related analogue(s)
- any protected derivative(s) and analogue(s)
- any activated derivative(s) and analogue(s)
- any resin-bound derivative(s) and analogue(s)
- any combination(s) of any of such salt, derivative and/or analogue types

of any of said compounds.

135. The compounds:

D/E/An-IRE-K/O/Ana, D/E/An-IRD-K/O/Ana, D/E/An-LRE-K/O/Ana, D/E/An-LRD-K/O/Ana, D/E/An-ERI-K/O/Ana, D/E/An-DRI-K/O/Ana, D/E/An-ERL-K/O/Ana, D/E/An-DRL-K/O/Ana, D/E/An-RIE-K/O/Ana, D/E/An-REI-K/O/Ana, D/E/An-IER-K/O/Ana, D/E/An-EIR-K/O/Ana, D/E/An-RLE-K/O/Ana, D/E/An-REL-K/O/Ana, D/E/An-LER-K/O/Ana, D/E/An-ELR-K/O/Ana, D/E/An-DIR-K/O/Ana, D/E/An-IDR-K/O/Ana, D/E/An-RDI-K/O/Ana, D/E/An-RID-K/O/Ana, D/E/An-DLR-K/O/Ana, D/E/An-LDR-K/O/Ana, D/E/An-RDL-K/O/Ana, D/E/An-RLD-K/O/Ana;

wherein:

D/E/An means aspartic acid or glutamic acid or a homolog thereof comprising no more than 12 carbon atoms, preferably aspartic acid or glutamic acid, and

K/O/Ana means lysine or ornithine or a homolog thereof comprising no more than 12 carbon atoms, preferably lysine or ornithine;

and wherein, between D/E/An and K/O/Ana, optionally:

a lactam bridge exists, and/or

a lactam bridge does not exist, and/or

the presence/number of lactam bridge(s) is undetermined and/or uncertain and/or fluctuating and/or variable and/or subject to change and/or fluctuation and/or uncomplete and/or partial;

and:

- any salt(s)
- any ester(s)
- any amide(s)
- any hydrazide(s)
- any *N*-substituted amide(s)
- any *N*-substituted hydrazide(s)
- any hydroxamic acid derivative(s)
- any decarboxylated analogue(s)
- any *N*-substituted derivative(s)
- any other related derivative(s)
- any other related analogue(s)
- any protected derivative(s) and analogue(s)
- any activated derivative(s) and analogue(s)
- any resin-bound derivative(s) and analogue(s)
- any combination(s) of any of such salt, derivative and/or analogue types

of any of the compounds as defined above.

136. The compounds:
K/O/Ana-IRE-D/E/An, K/O/Ana-IRD-D/E/An, K/O/Ana-LRE-D/E/An, K/O/Ana-LRD-D/E/An, K/O/Ana-ERI-D/E/An, K/O/Ana-DRI-D/E/An, K/O/Ana-ERL-D/E/An, K/O/Ana-DRL-D/E/An, K/O/Ana-RIE-D/E/An, K/O/Ana-REI-D/E/An, K/O/Ana-IER-D/E/An, K/O/Ana-EIR-D/E/An, K/O/Ana-RLE-D/E/An, K/O/Ana-REL-D/E/An, K/O/Ana-LER-D/E/An, K/O/Ana-ELR-D/E/An, K/O/Ana-DIR-D/E/An, K/O/Ana-IDR-D/E/An, K/O/Ana-RDI-D/E/An, K/O/Ana-RID-D/E/An, K/O/Ana-DLR-D/E/An, K/O/Ana-LDR-D/E/An, K/O/Ana-RDL-D/E/An, K/O/Ana-RLD-D/E/An;

wherein:

D/E/An means aspartic acid or glutamic acid or a homolog thereof comprising no more than 12 carbon atoms, preferably aspartic acid or glutamic acid, and

K/O/Ana means lysine or ornithine or a homolog thereof comprising no more than 12 carbon atoms, preferably lysine or ornithine;

and wherein, between K/O/Ana and D/E/An, optionally:
a lactam bridge exists, and/or
a lactam bridge does not exist, and/or
the presence/number of lactam bridge(s) is undetermined and/or uncertain and/or fluctuating and/or variable and/or subject to change and/or fluctuation and/or uncomplete and/or partial;

and:

- any salt(s)
- any ester(s)
- any amide(s)
- any hydrazide(s)
- any *N*-substituted amide(s)
- any *N*-substituted hydrazide(s)
- any hydroxamic acid derivative(s)
- any decarboxylated analogue(s)
- any *N*-substituted derivative(s)
- any other related derivative(s)
- any other related analogue(s)
- any protected derivative(s) and analogue(s)
- any activated derivative(s) and analogue(s)

- any resin-bound derivative(s) and analogue(s)
- any combination(s) of any of such salt, derivative and/or analogue types

of any of said compounds.

137. The compounds:

K/O/Ana-Ama-IRE-D/E/An, K/O/Ana-Ama-IRD-D/E/An, K/O/Ana-Ama-LRE-D/E/An, K/O/Ana-Ama-LRD-D/E/An, K/O/Ana-Ama-ERI-D/E/An, K/O/Ana-Ama-DRI-D/E/An, K/O/Ana-Ama-ERL-D/E/An, K/O/Ana-Ama-DRL-D/E/An, K/O/Ana-Ama-RIE-D/E/An, K/O/Ana-Ama-REI-D/E/An, K/O/Ana-Ama-IER-D/E/An, K/O/Ana-Ama-EIR-D/E/An, K/O/Ana-Ama-RLE-D/E/An, K/O/Ana-Ama-REL-D/E/An, K/O/Ana-Ama-LER-D/E/An, K/O/Ana-Ama-ELR-D/E/An, K/O/Ana-Ama-DIR-D/E/An, K/O/Ana-Ama-IDR-D/E/An, K/O/Ana-Ama-RDI-D/E/An, K/O/Ana-Ama-RID-D/E/An, K/O/Ana-Ama-DLR-D/E/An, K/O/Ana-Ama-LDR-D/E/An, K/O/Ana-Ama-RDL-D/E/An, K/O/Ana-Ama-RLD-D/E/An;

and the compounds:

K/O/Ana-Ama-Ama-IRE-D/E/An, K/O/Ana-Ama-Ama-IRD-D/E/An, K/O/Ana-Ama-Ama-LRE-D/E/An, K/O/Ana-Ama-Ama-LRD-D/E/An, K/O/Ana-Ama-Ama-ERI-D/E/An, K/O/Ana-Ama-Ama-DRI-D/E/An, K/O/Ana-Ama-Ama-ERL-D/E/An, K/O/Ana-Ama-Ama-DRL-D/E/An, K/O/Ana-Ama-Ama-RIE-D/E/An, K/O/Ana-Ama-Ama-REI-D/E/An, K/O/Ana-Ama-Ama-IER-D/E/An, K/O/Ana-Ama-Ama-EIR-D/E/An, K/O/Ana-Ama-Ama-RLE-D/E/An, K/O/Ana-Ama-Ama-REL-D/E/An, K/O/Ana-Ama-Ama-LER-D/E/An, K/O/Ana-Ama-Ama-ELR-D/E/An, K/O/Ana-Ama-Ama-DIR-D/E/An, K/O/Ana-Ama-Ama-IDR-D/E/An, K/O/Ana-Ama-Ama-RDI-D/E/An, K/O/Ana-Ama-Ama-RID-D/E/An, K/O/Ana-Ama-Ama-DLR-D/E/An, K/O/Ana-Ama-Ama-LDR-D/E/An, K/O/Ana-Ama-Ama-RDL-D/E/An, K/O/Ana-Ama-Ama-RLD-D/E/An;

and the compounds:

K/O/Ana-IRE-Ama-D/E/An, K/O/Ana-IRD-Ama-D/E/An, K/O/Ana-LRE-Ama-D/E/An, K/O/Ana-LRD-Ama-D/E/An, K/O/Ana-ERI-Ama-D/E/An, K/O/Ana-DRI-Ama-D/E/An, K/O/Ana-ERL-Ama-D/E/An, K/O/Ana-DRL-Ama-D/E/An, K/O/Ana-RIE-Ama-D/E/An, K/O/Ana-REI-Ama-D/E/An, K/O/Ana-IER-Ama-D/E/An, K/O/Ana-EIR-Ama-D/E/An, K/O/Ana-RLE-Ama-D/E/An, K/O/Ana-REL-Ama-D/E/An, K/O/Ana-LER-Ama-D/E/An, K/O/Ana-ELR-Ama-D/E/An, K/O/Ana-DIR-Ama-D/E/An, K/O/Ana-IDR-Ama-D/E/An, K/O/Ana-RDI-Ama-D/E/An, K/O/Ana-RID-Ama-D/E/An, K/O/Ana-DLR-Ama-D/E/An, K/O/Ana-LDR-Ama-D/E/An, K/O/Ana-RDL-Ama-D/E/An, K/O/Ana-RLD-Ama-D/E/An;

and the compounds:

K/O/Ana-IRE-Ama-Ama-D/E/An, K/O/Ana-IRD-Ama-Ama-D/E/An, K/O/Ana-LRE-Ama-Ama-D/E/An, K/O/Ana-LRD-Ama-Ama-D/E/An, K/O/Ana-ERI-Ama-Ama-D/E/An, K/O/Ana-DRI-Ama-Ama-D/E/An, K/O/Ana-ERL-Ama-Ama-D/E/An, K/O/Ana-DRL-Ama-Ama-D/E/An, K/O/Ana-RIE-Ama-Ama-D/E/An, K/O/Ana-REI-Ama-Ama-D/E/An, K/O/Ana-IER-Ama-Ama-D/E/An, K/O/Ana-EIR-Ama-Ama-D/E/An, K/O/Ana-RLE-Ama-Ama-D/E/An, K/O/Ana-REL-Ama-Ama-D/E/An, K/O/Ana-LER-Ama-Ama-D/E/An, K/O/Ana-ELR-Ama-Ama-D/E/An, K/O/Ana-DIR-Ama-Ama-D/E/An, K/O/Ana-IDR-Ama-Ama-D/E/An, K/O/Ana-RDI-Ama-Ama-D/E/An, K/O/Ana-RID-Ama-Ama-D/E/An, K/O/Ana-DLR-Ama-Ama-D/E/An, K/O/Ana-LDR-Ama-Ama-D/E/An, K/O/Ana-RDL-Ama-Ama-D/E/An, K/O/Ana-RLD-Ama-Ama-D/E/An;

and the compounds:

K/O/Ana-Ama-IRE-Ama-D/E/An, K/O/Ana-Ama-IRD-Ama-D/E/An, K/O/Ana-Ama-LRE-Ama-D/E/An, K/O/Ana-Ama-LRD-Ama-D/E/An, K/O/Ana-Ama-ERI-Ama-D/E/An, K/O/Ana-Ama-DRI-Ama-D/E/An, K/O/Ana-Ama-ERL-Ama-D/E/An, K/O/Ana-Ama-DRL-Ama-D/E/An, K/O/Ana-Ama-RIE-Ama-D/E/An, K/O/Ana-Ama-REI-Ama-D/E/An, K/O/Ana-Ama-IER-Ama-D/E/An, K/O/Ana-Ama-EIR-Ama-D/E/An, K/O/Ana-Ama-RLE-Ama-D/E/An, K/O/Ana-Ama-REL-Ama-D/E/An, K/O/Ana-Ama-LER-Ama-D/E/An, K/O/Ana-Ama-ELR-Ama-D/E/An, K/O/Ana-Ama-DIR-Ama-D/E/An, K/O/Ana-Ama-IDR-Ama-D/E/An, K/O/Ana-Ama-RDI-Ama-D/E/An, K/O/Ana-Ama-RID-Ama-D/E/An, K/O/Ana-Ama-DLR-Ama-D/E/An, K/O/Ana-Ama-LDR-Ama-D/E/An, K/O/Ana-Ama-RDL-Ama-D/E/An, K/O/Ana-Ama-RLD-Ama-D/E/An;

and the compounds:

K/O/Ana-Ama-IRE-Ama-Ama-D/E/An, K/O/Ana-Ama-IRD-Ama-Ama-D/E/An, K/O/Ana-Ama-LRE-Ama-Ama-D/E/An, K/O/Ana-Ama-LRD-Ama-Ama-D/E/An, K/O/Ana-Ama-ERI-Ama-Ama-D/E/An, K/O/Ana-Ama-DRI-Ama-Ama-D/E/An, K/O/Ana-Ama-ERL-Ama-Ama-D/E/An, K/O/Ana-Ama-DRL-Ama-Ama-D/E/An, K/O/Ana-Ama-RIE-Ama-Ama-D/E/An, K/O/Ana-Ama-REI-Ama-Ama-D/E/An, K/O/Ana-Ama-IER-Ama-Ama-D/E/An, K/O/Ana-Ama-EIR-Ama-Ama-D/E/An, K/O/Ana-Ama-RLE-Ama-Ama-D/E/An, K/O/Ana-Ama-REL-Ama-Ama-D/E/An, K/O/Ana-Ama-LER-Ama-Ama-D/E/An, K/O/Ana-Ama-ELR-Ama-Ama-D/E/An, K/O/Ana-Ama-DIR-Ama-Ama-D/E/An, K/O/Ana-Ama-IDR-Ama-Ama-D/E/An, K/O/Ana-Ama-RDI-Ama-Ama-D/E/An, K/O/Ana-Ama-RID-Ama-Ama-D/E/An,

K/O/Ana-Ama-DLR-Ama-Ama-D/E/An, K/O/Ana-Ama-LDR-Ama-Ama-D/E/An, K/O/Ana-Ama-RDL-Ama-Ama-D/E/An, K/O/Ana-Ama-RLD-Ama-Ama-D/E/An;

and the compounds:

K/O/Ana-Ama-Ama-IRE-Ama-D/E/An, K/O/Ana-Ama-Ama-IRD-Ama-D/E/An, K/O/Ana-Ama-Ama-LRE-Ama-D/E/An, K/O/Ana-Ama-Ama-LRD-Ama-D/E/An, K/O/Ana-Ama-Ama-ERI-Ama-D/E/An, K/O/Ana-Ama-Ama-DRI-Ama-D/E/An, K/O/Ana-Ama-Ama-ERL-Ama-D/E/An, K/O/Ana-Ama-Ama-DRL-Ama-D/E/An, K/O/Ana-Ama-Ama-RIE-Ama-D/E/An, K/O/Ana-Ama-Ama-REI-Ama-D/E/An, K/O/Ana-Ama-Ama-IER-Ama-D/E/An, K/O/Ana-Ama-Ama-EIR-Ama-D/E/An, K/O/Ana-Ama-Ama-RLE-Ama-D/E/An, K/O/Ana-Ama-Ama-REL-Ama-D/E/An, K/O/Ana-Ama-Ama-LER-Ama-D/E/An, K/O/Ana-Ama-Ama-ELR-Ama-D/E/An, K/O/Ana-Ama-Ama-DIR-Ama-D/E/An, K/O/Ana-Ama-Ama-IDR-Ama-D/E/An, K/O/Ana-Ama-Ama-RDI-Ama-D/E/An, K/O/Ana-Ama-Ama-RID-Ama-D/E/An, K/O/Ana-Ama-Ama-DLR-Ama-D/E/An, K/O/Ana-Ama-Ama-LDR-Ama-D/E/An, K/O/Ana-Ama-Ama-RDL-Ama-D/E/An, K/O/Ana-Ama-Ama-RLD-Ama-D/E/An;

and the compounds:

K/O/Ana-Ama-Ama-IRE-Ama-Ama-D/E/An, K/O/Ana-Ama-Ama-IRD-Ama-Ama-D/E/An, K/O/Ana-Ama-Ama-LRE-Ama-Ama-D/E/An, K/O/Ana-Ama-Ama-LRD-Ama-Ama-D/E/An, K/O/Ana-Ama-Ama-ERI-Ama-Ama-D/E/An, K/O/Ana-Ama-Ama-DRI-Ama-Ama-D/E/An, K/O/Ana-Ama-Ama-ERL-Ama-Ama-D/E/An, K/O/Ana-Ama-Ama-DRL-Ama-Ama-D/E/An, K/O/Ana-Ama-Ama-RIE-Ama-Ama-D/E/An, K/O/Ana-Ama-Ama-REI-Ama-Ama-D/E/An, K/O/Ana-Ama-Ama-IER-Ama-Ama-D/E/An, K/O/Ana-Ama-Ama-EIR-Ama-Ama-D/E/An, K/O/Ana-Ama-Ama-RLE-Ama-Ama-D/E/An, K/O/Ana-Ama-Ama-REL-Ama-Ama-D/E/An, K/O/Ana-Ama-Ama-LER-Ama-Ama-D/E/An, K/O/Ana-Ama-Ama-ELR-Ama-Ama-D/E/An, K/O/Ana-Ama-Ama-DIR-Ama-Ama-D/E/An, K/O/Ana-Ama-Ama-IDR-Ama-Ama-D/E/An, K/O/Ana-Ama-Ama-RDI-Ama-Ama-D/E/An, K/O/Ana-Ama-Ama-RID-Ama-Ama-D/E/An, K/O/Ana-Ama-Ama-DLR-Ama-Ama-D/E/An, K/O/Ana-Ama-Ama-LDR-Ama-Ama-D/E/An, K/O/Ana-Ama-Ama-RDL-Ama-Ama-D/E/An, K/O/Ana-Ama-Ama-RLD-Ama-Ama-D/E/An;

wherein:

D/E/An means aspartic acid or glutamic acid or a homolog thereof comprising no more than 12 carbon atoms, preferably aspartic acid or glutamic acid, and

K/O/Ana means lysine or ornithine or a homolog thereof comprising no more than 12 carbon atoms, preferably lysine or ornithine, and

each Ama, independently, means a natural amino acid residue or any unnatural amino acid residue comprising maximally 30 non-hydrogen atoms and an unlimited number of hydrogen atoms;

and wherein, between K/O/Ana and D/E/An, optionally:

a lactam bridge exists, and/or
a lactam bridge does not exist, and/or
the presence/number of lactam bridge(s) is undetermined and/or uncertain and/or fluctuating and/or variable and/or subject to change and/or fluctuation and/or uncomplete and/or partial;

and:

- any salt(s)
- any ester(s)
- any amide(s)
- any hydrazide(s)
- any *N*-substituted amide(s)
- any *N*-substituted hydrazide(s)
- any hydroxamic acid derivative(s)
- any decarboxylated analogue(s)
- any *N*-substituted derivative(s)
- any other related derivative(s)
- any other related analogue(s)
- any protected derivative(s) and analogue(s)
- any activated derivative(s) and analogue(s)
- any resin-bound derivative(s) and analogue(s)
- any combination(s) of any of such salt, derivative and/or analogue types

of any of said compounds.

138. The compounds:

D/E/An-Ama-IRE-K/O/Ana, D/E/An-Ama-IRD-K/O/Ana, D/E/An-Ama-LRE-K/O/Ana, D/E/An-Ama-LRD-K/O/Ana, D/E/An-Ama-ERI-K/O/Ana, D/E/An-Ama-DRI-K/O/Ana, D/E/An-Ama-ERL-K/O/Ana, D/E/An-Ama-DRL-K/O/Ana, D/E/An-Ama-RIE-K/O/Ana,

D/E/An-Ama-REI-K/O/Ana, D/E/An-Ama-IER-K/O/Ana, D/E/An-Ama-EIR-K/O/Ana, D/E/An-Ama-RLE-K/O/Ana, D/E/An-Ama-REL-K/O/Ana, D/E/An-Ama-LER-K/O/Ana, D/E/An-Ama-ELR-K/O/Ana, D/E/An-Ama-DIR-K/O/Ana, D/E/An-Ama-IDR-K/O/Ana, D/E/An-Ama-RDI-K/O/Ana, D/E/An-Ama-RID-K/O/Ana, D/E/An-Ama-DLR-K/O/Ana, D/E/An-Ama-LDR-K/O/Ana, D/E/An-Ama-RDL-K/O/Ana, D/E/An-Ama-RLD-K/O/Ana;

and the compounds:

D/E/An-Ama-Ama-IRE-K/O/Ana, D/E/An-Ama-Ama-IRD-K/O/Ana, D/E/An-Ama-Ama-LRE-K/O/Ana, D/E/An-Ama-Ama-LRD-K/O/Ana, D/E/An-Ama-Ama-ERI-K/O/Ana, D/E/An-Ama-Ama-DRI-K/O/Ana, D/E/An-Ama-Ama-ERL-K/O/Ana, D/E/An-Ama-Ama-DRL-K/O/Ana, D/E/An-Ama-Ama-RIE-K/O/Ana, D/E/An-Ama-Ama-REI-K/O/Ana, D/E/An-Ama-Ama-IER-K/O/Ana, D/E/An-Ama-Ama-EIR-K/O/Ana, D/E/An-Ama-Ama-RLE-K/O/Ana, D/E/An-Ama-Ama-REL-K/O/Ana, D/E/An-Ama-Ama-LER-K/O/Ana, D/E/An-Ama-Ama-ELR-K/O/Ana, D/E/An-Ama-Ama-DIR-K/O/Ana, D/E/An-Ama-Ama-IDR-K/O/Ana, D/E/An-Ama-Ama-RDI-K/O/Ana, D/E/An-Ama-Ama-RID-K/O/Ana, D/E/An-Ama-Ama-DLR-K/O/Ana, D/E/An-Ama-Ama-LDR-K/O/Ana, D/E/An-Ama-Ama-RDL-K/O/Ana, D/E/An-Ama-Ama-RLD-K/O/Ana;

and the compounds:

D/E/An-IRE-Ama-K/O/Ana, D/E/An-IRD-Ama-K/O/Ana, D/E/An-LRE-Ama-K/O/Ana, D/E/An-LRD-Ama-K/O/Ana, D/E/An-ERI-Ama-K/O/Ana, D/E/An-DRI-Ama-K/O/Ana, D/E/An-ERL-Ama-K/O/Ana, D/E/An-DRL-Ama-K/O/Ana, D/E/An-RIE-Ama-K/O/Ana, D/E/An-REI-Ama-K/O/Ana, D/E/An-IER-Ama-K/O/Ana, D/E/An-EIR-Ama-K/O/Ana, D/E/An-RLE-Ama-K/O/Ana, D/E/An-REL-Ama-K/O/Ana, D/E/An-LER-Ama-K/O/Ana, D/E/An-ELR-Ama-K/O/Ana, D/E/An-DIR-Ama-K/O/Ana, D/E/An-IDR-Ama-K/O/Ana, D/E/An-RDI-Ama-K/O/Ana, D/E/An-RID-Ama-K/O/Ana, D/E/An-DLR-Ama-K/O/Ana, D/E/An-LDR-Ama-K/O/Ana, D/E/An-RDL-Ama-K/O/Ana, D/E/An-RLD-Ama-K/O/Ana;

and the compounds:

D/E/An-IRE-Ama-Ama-K/O/Ana, D/E/An-IRD-Ama-Ama-K/O/Ana, D/E/An-LRE-Ama-Ama-K/O/Ana, D/E/An-LRD-Ama-Ama-K/O/Ana, D/E/An-ERI-Ama-Ama-K/O/Ana, D/E/An-DRI-Ama-Ama-K/O/Ana, D/E/An-ERL-Ama-Ama-K/O/Ana, D/E/An-DRL-Ama-Ama-K/O/Ana, D/E/An-RIE-Ama-Ama-K/O/Ana, D/E/An-REI-Ama-Ama-K/O/Ana, D/E/An-IER-Ama-Ama-K/O/Ana, D/E/An-EIR-Ama-Ama-K/O/Ana, D/E/An-RLE-Ama-Ama-K/O/Ana, D/E/An-REL-Ama-Ama-K/O/Ana, D/E/An-LER-Ama-Ama-K/O/Ana, D/E/An-ELR-Ama-Ama-K/O/Ana, D/E/An-DIR-Ama-Ama-K/O/Ana, D/E/An-IDR-Ama-

Ama-K/O/Ana, D/E/An-RDI-Ama-Ama-K/O/Ana, D/E/An-RID-Ama-Ama-K/O/Ana, D/E/An-DLR-Ama-Ama-K/O/Ana, D/E/An-LDR-Ama-Ama-K/O/Ana, D/E/An-RDL-Ama-Ama-K/O/Ana, D/E/An-RLD-Ama-Ama-K/O/Ana;

and the compounds:

D/E/An-Ama-IRE-Ama-K/O/Ana, D/E/An-Ama-IRD-Ama-K/O/Ana, D/E/An-Ama-LRE-Ama-K/O/Ana, D/E/An-Ama-LRD-Ama-K/O/Ana, D/E/An-Ama-ERI-Ama-K/O/Ana, D/E/An-Ama-DRI-Ama-K/O/Ana, D/E/An-Ama-ERL-Ama-K/O/Ana, D/E/An-Ama-DRL-Ama-K/O/Ana, D/E/An-Ama-RIE-Ama-K/O/Ana, D/E/An-Ama-REI-Ama-K/O/Ana, D/E/An-Ama-IER-Ama-K/O/Ana, D/E/An-Ama-EIR-Ama-K/O/Ana, D/E/An-Ama-RLE-Ama-K/O/Ana, D/E/An-Ama-REL-Ama-K/O/Ana, D/E/An-Ama-LER-Ama-K/O/Ana, D/E/An-Ama-ELR-Ama-K/O/Ana, D/E/An-Ama-DIR-Ama-K/O/Ana, D/E/An-Ama-IDR-Ama-K/O/Ana, D/E/An-Ama-RDI-Ama-K/O/Ana, D/E/An-Ama-RID-Ama-K/O/Ana, D/E/An-Ama-DLR-Ama-K/O/Ana, D/E/An-Ama-LDR-Ama-K/O/Ana, D/E/An-Ama-RDL-Ama-K/O/Ana, D/E/An-Ama-RLD-Ama-K/O/Ana;

and the compounds:

D/E/An-Ama-IRE-Ama-Ama-K/O/Ana, D/E/An-Ama-IRD-Ama-Ama-K/O/Ana, D/E/An-Ama-LRE-Ama-Ama-K/O/Ana, D/E/An-Ama-LRD-Ama-Ama-K/O/Ana, D/E/An-Ama-ERI-Ama-Ama-K/O/Ana, D/E/An-Ama-DRI-Ama-Ama-K/O/Ana, D/E/An-Ama-ERL-Ama-Ama-K/O/Ana, D/E/An-Ama-DRL-Ama-Ama-K/O/Ana, D/E/An-Ama-RIE-Ama-Ama-K/O/Ana, D/E/An-Ama-REI-Ama-Ama-K/O/Ana, D/E/An-Ama-IER-Ama-Ama-K/O/Ana, D/E/An-Ama-EIR-Ama-Ama-K/O/Ana, D/E/An-Ama-RLE-Ama-Ama-K/O/Ana, D/E/An-Ama-REL-Ama-Ama-K/O/Ana, D/E/An-Ama-LER-Ama-Ama-K/O/Ana, D/E/An-Ama-ELR-Ama-Ama-K/O/Ana, D/E/An-Ama-DIR-Ama-Ama-K/O/Ana, D/E/An-Ama-IDR-Ama-Ama-K/O/Ana, D/E/An-Ama-RDI-Ama-Ama-K/O/Ana, D/E/An-Ama-RID-Ama-Ama-K/O/Ana, D/E/An-Ama-DLR-Ama-Ama-K/O/Ana, D/E/An-Ama-LDR-Ama-Ama-K/O/Ana, D/E/An-Ama-RDL-Ama-Ama-K/O/Ana, D/E/An-Ama-RLD-Ama-Ama-K/O/Ana;

and the compounds:

D/E/An-Ama-Ama-IRE-Ama-K/O/Ana, D/E/An-Ama-Ama-IRD-Ama-K/O/Ana, D/E/An-Ama-Ama-LRE-Ama-K/O/Ana, D/E/An-Ama-Ama-LRD-Ama-K/O/Ana, D/E/An-Ama-Ama-ERI-Ama-K/O/Ana, D/E/An-Ama-Ama-DRI-Ama-K/O/Ana, D/E/An-Ama-Ama-ERL-Ama-K/O/Ana, D/E/An-Ama-Ama-DRL-Ama-K/O/Ana, D/E/An-Ama-Ama-RIE-Ama-K/O/Ana, D/E/An-Ama-Ama-REI-Ama-K/O/Ana, D/E/An-Ama-Ama-IER-Ama-

K/O/Ana, D/E/An-Ama-Ama-EIR-Ama-K/O/Ana, D/E/An-Ama-Ama-RLE-Ama-K/O/Ana, D/E/An-Ama-Ama-REL-Ama-K/O/Ana, D/E/An-Ama-Ama-LER-Ama-K/O/Ana, D/E/An-Ama-Ama-ELR-Ama-K/O/Ana, D/E/An-Ama-Ama-DIR-Ama-K/O/Ana, D/E/An-Ama-Ama-IDR-Ama-K/O/Ana, D/E/An-Ama-Ama-RDI-Ama-K/O/Ana, D/E/An-Ama-Ama-RID-Ama-K/O/Ana, D/E/An-Ama-Ama-DLR-Ama-K/O/Ana, D/E/An-Ama-Ama-LDR-Ama-K/O/Ana, D/E/An-Ama-Ama-RDL-Ama-K/O/Ana, D/E/An-Ama-Ama-RLD-Ama-K/O/Ana;

and the compounds:

D/E/An-Ama-Ama-IRE-Ama-Ama-K/O/Ana, D/E/An-Ama-Ama-IRD-Ama-Ama-K/O/Ana, D/E/An-Ama-Ama-LRE-Ama-Ama-K/O/Ana, D/E/An-Ama-Ama-LRD-Ama-Ama-K/O/Ana, D/E/An-Ama-Ama-ERI-Ama-Ama-K/O/Ana, D/E/An-Ama-Ama-DRI-Ama-Ama-K/O/Ana, D/E/An-Ama-Ama-ERL-Ama-Ama-K/O/Ana, D/E/An-Ama-Ama-DRL-Ama-Ama-K/O/Ana, D/E/An-Ama-Ama-RIE-Ama-Ama-K/O/Ana, D/E/An-Ama-Ama-REI-Ama-Ama-K/O/Ana, D/E/An-Ama-Ama-IER-Ama-Ama-K/O/Ana, D/E/An-Ama-Ama-EIR-Ama-Ama-K/O/Ana, D/E/An-Ama-Ama-RLE-Ama-Ama-K/O/Ana, D/E/An-Ama-Ama-REL-Ama-Ama-K/O/Ana, D/E/An-Ama-Ama-LER-Ama-Ama-K/O/Ana, D/E/An-Ama-Ama-ELR-Ama-Ama-K/O/Ana, D/E/An-Ama-Ama-DIR-Ama-Ama-K/O/Ana, D/E/An-Ama-Ama-IDR-Ama-Ama-K/O/Ana, D/E/An-Ama-Ama-RDI-Ama-Ama-K/O/Ana, D/E/An-Ama-Ama-RID-Ama-Ama-K/O/Ana, D/E/An-Ama-Ama-DLR-Ama-Ama-K/O/Ana, D/E/An-Ama-Ama-LDR-Ama-Ama-K/O/Ana, D/E/An-Ama-Ama-RDL-Ama-Ama-K/O/Ana, D/E/An-Ama-Ama-RLD-Ama-Ama-K/O/Ana;

wherein:

D/E/An means aspartic acid or glutamic acid or a homolog thereof comprising no more than 12 carbon atoms, preferably aspartic acid or glutamic acid, and

K/O/Ana means lysine or ornithine or a homolog thereof comprising no more than 12 carbon atoms, preferably lysine or ornithine, and

each Ama, independently, means a natural amino acid residue or any unnatural amino acid residue comprising maximally 30 non-hydrogen atoms and an unlimited number of hydrogen atoms;

and wherein, between K/O/Ana and D/E/An, optionally:

a lactam bridge exists, and/or

a lactam bridge does not exist, and/or
the presence/number of lactam bridge(s) is undetermined and/or uncertain and/or fluctuating and/or variable and/or subject to change and/or fluctuation and/or uncomplete and/or partial;

and:

- any salt(s)
- any ester(s)
- any amide(s)
- any hydrazide(s)
- any *N*-substituted amide(s)
- any *N*-substituted hydrazide(s)
- any hydroxamic acid derivative(s)
- any decarboxylated analogue(s)
- any *N*-substituted derivative(s)
- any other related derivative(s)
- any other related analogue(s)
- any protected derivative(s) and analogue(s)
- any activated derivative(s) and analogue(s)
- any resin-bound derivative(s) and analogue(s)
- any combination(s) of any of such salt, derivative and/or analogue types

of any of said compounds.

139. The compounds:

K/O/Ana-Peptseq-IRE-D/E/An, K/O/Ana-Peptseq-IRD-D/E/An, K/O/Ana-Peptseq-LRE-D/E/An, K/O/Ana-Peptseq-LRD-D/E/An, K/O/Ana-Peptseq-ERI-D/E/An, K/O/Ana-Peptseq-DRI-D/E/An, K/O/Ana-Peptseq-ERL-D/E/An, K/O/Ana-Peptseq-DRL-D/E/An, K/O/Ana-Peptseq-RIE-D/E/An, K/O/Ana-Peptseq-REI-D/E/An, K/O/Ana-Peptseq-IER-D/E/An, K/O/Ana-Peptseq-EIR-D/E/An, K/O/Ana-Peptseq-RLE-D/E/An, K/O/Ana-Peptseq-REL-D/E/An, K/O/Ana-Peptseq-LER-D/E/An, K/O/Ana-Peptseq-ELR-D/E/An, K/O/Ana-Peptseq-DIR-D/E/An, K/O/Ana-Peptseq-IDR-D/E/An, K/O/Ana-Peptseq-RDI-D/E/An, K/O/Ana-Peptseq-RID-D/E/An, K/O/Ana-Peptseq-DLR-D/E/An, K/O/Ana-Peptseq-LDR-D/E/An, K/O/Ana-Peptseq-RDL-D/E/An, K/O/Ana-Peptseq-RLD-D/E/An;

and the compounds:

K/O/Ana-IRE-Peptseq-D/E/An, K/O/Ana-IRD-Peptseq-D/E/An, K/O/Ana-LRE-Peptseq-

D/E/An, K/O/Ana-LRD-Peptseq-D/E/An, K/O/Ana-ERI-Peptseq-D/E/An, K/O/Ana-DRI-Peptseq-D/E/An, K/O/Ana-ERL-Peptseq-D/E/An, K/O/Ana-DRL-Peptseq-D/E/An, K/O/Ana-RIE-Peptseq-D/E/An, K/O/Ana-REI-Peptseq-D/E/An, K/O/Ana-IER-Peptseq-D/E/An, K/O/Ana-EIR-Peptseq-D/E/An, K/O/Ana-RLE-Peptseq-D/E/An, K/O/Ana-REL-Peptseq-D/E/An, K/O/Ana-LER-Peptseq-D/E/An, K/O/Ana-ELR-Peptseq-D/E/An, K/O/Ana-DIR-Peptseq-D/E/An, K/O/Ana-IDR-Peptseq-D/E/An, K/O/Ana-RDI-Peptseq-D/E/An, K/O/Ana-RID-Peptseq-D/E/An, K/O/Ana-DLR-Peptseq-D/E/An, K/O/Ana-LDR-Peptseq-D/E/An, K/O/Ana-RDL-Peptseq-D/E/An, K/O/Ana-RLD-Peptseq-D/E/An;

and the compounds:

K/O/Ana-Peptseq-IRE-Peptseq-D/E/An, K/O/Ana-Peptseq-IRD-Peptseq-D/E/An, K/O/Ana-Peptseq-LRE-Peptseq-D/E/An, K/O/Ana-Peptseq-LRD-Peptseq-D/E/An, K/O/Ana-Peptseq-ERI-Peptseq-D/E/An, K/O/Ana-Peptseq-DRI-Peptseq-D/E/An, K/O/Ana-Peptseq-ERL-Peptseq-D/E/An, K/O/Ana-Peptseq-DRL-Peptseq-D/E/An, K/O/Ana-Peptseq-RIE-Peptseq-D/E/An, K/O/Ana-Peptseq-REI-Peptseq-D/E/An, K/O/Ana-Peptseq-IER-Peptseq-D/E/An, K/O/Ana-Peptseq-EIR-Peptseq-D/E/An, K/O/Ana-Peptseq-RLE-Peptseq-D/E/An, K/O/Ana-Peptseq-REL-Peptseq-D/E/An, K/O/Ana-Peptseq-LER-Peptseq-D/E/An, K/O/Ana-Peptseq-ELR-Peptseq-D/E/An, K/O/Ana-Peptseq-DIR-Peptseq-D/E/An, K/O/Ana-Peptseq-IDR-Peptseq-D/E/An, K/O/Ana-Peptseq-RDI-Peptseq-D/E/An, K/O/Ana-Peptseq-RID-Peptseq-D/E/An, K/O/Ana-Peptseq-DLR-Peptseq-D/E/An, K/O/Ana-Peptseq-LDR-Peptseq-D/E/An, K/O/Ana-Peptseq-RDL-Peptseq-D/E/An, K/O/Ana-Peptseq-RLD-Peptseq-D/E/An;

wherein:

D/E/An means aspartic acid or glutamic acid or a homolog thereof comprising no more than 12 carbon atoms, preferably aspartic acid or glutamic acid, and

K/O/Ana means lysine or ornithine or a homolog thereof comprising no more than 12 carbon atoms, preferably lysine or ornithine, and

each Peptseq, independently, means: a natural amino acid residue; or an unnatural amino acid residue comprising maximally 30 non-hydrogen atoms and an unlimited number of hydrogen atoms; or a sequence of 2 to 25, prefereably 2 to 12, more preferably 2 to 6, still more preferably 2 to 4, and most preferably 3, amino acid residues (peptide units), wherein the amino acid residues are natural amino acid residue(s) and/or unnatural amino acid residue(s) comprising maximally 30 non-hydrogen atoms and an unlimited

number of hydrogen atoms;

and wherein in each compound at least one, and preferably only one, Peptseq comprises 3 to 25, prefereably 3 to 12, more preferably 3 to 6, still more preferably 3 to 4, and most preferably 3, amino acid residues (peptide units);

and wherein, between K/O/Ana and D/E/An, optionally:
a lactam bridge exists, and/or
a lactam bridge does not exist, and/or
the presence/number of lactam bridge(s) is undetermined and/or uncertain and/or fluctuating and/or variable and/or subject to change and/or fluctuation and/or uncomplete and/or partial;

and:

- any salt(s)
- any ester(s)
- any amide(s)
- any hydrazide(s)
- any *N*-substituted amide(s)
- any *N*-substituted hydrazide(s)
- any hydroxamic acid derivative(s)
- any decarboxylated analogue(s)
- any *N*-substituted derivative(s)
- any other related derivative(s)
- any other related analogue(s)
- any protected derivative(s) and analogue(s)
- any activated derivative(s) and analogue(s)
- any resin-bound derivative(s) and analogue(s)
- any combination(s) of any of such salt, derivative and/or analogue types

of any of said compounds.

140. Compounds that have the structural formula

Pe-Cy-Dd-Ee-Ff-Cyy-Pep

wherein Cy, Dd-Ee-Ff and Cyy are as defined in claim 123 and/or as defined in claim 125 and/or as defined in any one of claims 127 to 131

and/or the structural formula

Pe-Cy-Rr^1-Rr^2-...-Rr^n-Cyy-Pep

wherein Cy, Rr^1-Rr^2-...-Rr^n and Cyy are as defined in claim 124 and/or as defined in claim 126 and/or as defined in any one of claims 128 to 131;

and wherein Pe and Pep, independently of each other and independently of any other structural unit(s)/part(s), are selected from the group of:

natural amino acids/amino acid residues, and

unnatural amino acids/amino acid residues that comprise maximally 35 non-hydrogen atoms and an unlimited number of hydrogen atoms each, and

peptide sequences/residues comprising 2 to 25, preferably 2 to 10, more preferably 2 to 6, and most preferably 2 to 4, natural amino acids/amino acid residues and/or unnatural amino acids/amino acid residues that each comprise maximally 35 non-hydrogen atoms and an unlimited number of hydrogen atoms;

and/or: Pe means that Cy is unsubstituted (absence of substituent(s); hydrogen) or Pep means that Cyy is unsubstituted (absence of substituent(s); hydrogen);

and wherein any amino acid(s) may comprise L amino acid(s) and/or D amino acid(s) and/or any other optical isomer(s);

and wherein the compounds Cy-Dd-Ee-Ff-Cyy may and/or may not be cyclic, and/or the amount and/or location(s) of cyclic structure(s) may vary and/or change;

and:

- any salt(s)
- any ester(s)
- any amide(s)
- any hydrazide(s)
- any *N*-substituted amide(s)
- any *N*-substituted hydrazide(s)
- any hydroxamic acid derivative(s)
- any decarboxylated analogue(s)
- any *N*-substituted derivative(s)
- any other related derivative(s)

- any other related analogue(s)
- any protected derivative(s) and analogue(s)
- any activated derivative(s) and analogue(s)
- any resin-bound derivative(s) and analogue(s)
- any combination(s) of any of such salt, derivative and/or analogue types

of any of said compounds.

141. The compounds:

Pe-CIREC-Pep, Pe-CIRDC-Pep, Pe-CLREC-Pep, Pe-CLRDC-Pep, Pe-CERIC-Pep, Pe-CDRIC-Pep, Pe-CERLC-Pep, Pe-CDRLC-Pep, Pe-CRIEC-Pep, Pe-CREIC-Pep, Pe-CIERC-Pep, Pe-CEIRC-Pep, Pe-CRLEC-Pep, Pe-CRELC-Pep, Pe-CLERC-Pep, Pe-CELRC-Pep, Pe-CDIRC-Pep, Pe-CIDRC-Pep, Pe-CRDIC-Pep, Pe-CRIDC-Pep, Pe-CDLRC-Pep, Pe-CLDRC-Pep, Pe-CRDLC-Pep and Pe-CRLDC-Pep;

and the compounds:

Pe-D/E/An-IRE-K/O/Ana-Pep, Pe-D/E/An-IRD-K/O/Ana-Pep, Pe-D/E/An-LRE-K/O/Ana-Pep, Pe-D/E/An-LRD-K/O/Ana-Pep, Pe-D/E/An-ERI-K/O/Ana-Pep, Pe-D/E/An-DRI-K/O/Ana-Pep, Pe-D/E/An-ERL-K/O/Ana-Pep, Pe-D/E/An-DRL-K/O/Ana-Pep, Pe-D/E/An-RIE-K/O/Ana-Pep, Pe-D/E/An-REI-K/O/Ana-Pep, Pe-D/E/An-IER-K/O/Ana-Pep, Pe-D/E/An-EIR-K/O/Ana-Pep, Pe-D/E/An-RLE-K/O/Ana-Pep, Pe-D/E/An-REL-K/O/Ana-Pep, Pe-D/E/An-LER-K/O/Ana-Pep, Pe-D/E/An-ELR-K/O/Ana-Pep, Pe-D/E/An-DIR-K/O/Ana-Pep, Pe-D/E/An-IDR-K/O/Ana-Pep, Pe-D/E/An-RDI-K/O/Ana-Pep, Pe-D/E/An-RID-K/O/Ana-Pep, Pe-D/E/An-DLR-K/O/Ana-Pep, Pe-D/E/An-LDR-K/O/Ana-Pep, Pe-D/E/An-RDL-K/O/Ana-Pep, Pe-D/E/An-RLD-K/O/Ana-Pep; wherein D/E/An and K/O/Ana are as defined in claim 135 and/or any other one(s) of the previous claims;

and the compounds:

Pe-K/O/Ana-IRE-D/E/An-Pep, Pe-K/O/Ana-IRD-D/E/An-Pep, Pe-K/O/Ana-LRE-D/E/An-Pep, Pe-K/O/Ana-LRD-D/E/An-Pep, Pe-K/O/Ana-ERI-D/E/An-Pep, Pe-K/O/Ana-DRI-D/E/An-Pep, Pe-K/O/Ana-ERL-D/E/An-Pep, Pe-K/O/Ana-DRL-D/E/An-Pep, Pe-K/O/Ana-RIE-D/E/An-Pep, Pe-K/O/Ana-REI-D/E/An-Pep, Pe-K/O/Ana-IER-D/E/An-Pep, Pe-K/O/Ana-EIR-D/E/An-Pep, Pe-K/O/Ana-RLE-D/E/An-Pep, Pe-K/O/Ana-REL-D/E/An-Pep, Pe-K/O/Ana-LER-D/E/An-Pep, Pe-K/O/Ana-ELR-D/E/An-Pep, Pe-K/O/Ana-DIR-D/E/An-Pep, Pe-K/O/Ana-IDR-D/E/An-Pep, Pe-K/O/Ana-RDI-D/E/An-Pep, Pe-K/O/Ana-RID-D/E/An-Pep, Pe-K/O/Ana-DLR-D/E/An-Pep, Pe-K/O/Ana-LDR-D/E/An-Pep, Pe-

K/O/Ana-RDL-D/E/An-Pep, Pe-K/O/Ana-RLD-D/E/An-Pep; wherein D/E/An and K/O/Ana are as defined in claim 136 and/or any other one(s) of the previous claims;

and the compounds:

Pe-K/O/Ana-Ama-IRE-D/E/An-Pep, Pe-K/O/Ana-Ama-IRD-D/E/An-Pep, Pe-K/O/Ana-Ama-LRE-D/E/An-Pep, Pe-K/O/Ana-Ama-LRD-D/E/An-Pep, Pe-K/O/Ana-Ama-ERI-D/E/An-Pep, Pe-K/O/Ana-Ama-DRI-D/E/An-Pep, Pe-K/O/Ana-Ama-ERL-D/E/An-Pep, Pe-K/O/Ana-Ama-DRL-D/E/An-Pep, Pe-K/O/Ana-Ama-RIE-D/E/An-Pep, Pe-K/O/Ana-Ama-REI-D/E/An-Pep, Pe-K/O/Ana-Ama-IER-D/E/An-Pep, Pe-K/O/Ana-Ama-EIR-D/E/An-Pep, Pe-K/O/Ana-Ama-RLE-D/E/An-Pep, Pe-K/O/Ana-Ama-REL-D/E/An-Pep, Pe-K/O/Ana-Ama-LER-D/E/An-Pep, Pe-K/O/Ana-Ama-ELR-D/E/An-Pep, Pe-K/O/Ana-Ama-DIR-D/E/An-Pep, Pe-K/O/Ana-Ama-IDR-D/E/An-Pep, Pe-K/O/Ana-Ama-RDI-D/E/An-Pep, Pe-K/O/Ana-Ama-RID-D/E/An-Pep, Pe-K/O/Ana-Ama-DLR-D/E/An-Pep, Pe-K/O/Ana-Ama-LDR-D/E/An-Pep, Pe-K/O/Ana-Ama-RDL-D/E/An-Pep, Pe-K/O/Ana-Ama-RLD-D/E/An-Pep; wherein D/E/An, K/O/Ana and Ama are as defined in claim 137 and/or any other one(s) of the previous claims;

and the compounds:

Pe-K/O/Ana-Ama-Ama-IRE-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-IRD-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-LRE-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-LRD-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-ERI-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-DRI-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-ERL-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-DRL-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-RIE-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-REI-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-IER-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-EIR-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-RLE-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-REL-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-LER-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-ELR-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-DIR-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-IDR-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-RDI-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-RID-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-DLR-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-LDR-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-RDL-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-RLD-D/E/An-Pep; wherein D/E/An, K/O/Ana and Ama are as defined in claim 137 and/or any other one(s) of the previous claims;

and the compounds:

Pe-K/O/Ana-IRE-Ama-D/E/An-Pep, Pe-K/O/Ana-IRD-Ama-D/E/An-Pep, Pe-K/O/Ana-LRE-Ama-D/E/An-Pep, Pe-K/O/Ana-LRD-Ama-D/E/An-Pep, Pe-K/O/Ana-ERI-Ama-

D/E/An-Pep, Pe-K/O/Ana-DRI-Ama-D/E/An-Pep, Pe-K/O/Ana-ERL-Ama-D/E/An-Pep, Pe-K/O/Ana-DRL-Ama-D/E/An-Pep, Pe-K/O/Ana-RIE-Ama-D/E/An-Pep, Pe-K/O/Ana-REI-Ama-D/E/An-Pep, Pe-K/O/Ana-IER-Ama-D/E/An-Pep, Pe-K/O/Ana-EIR-Ama-D/E/An-Pep, Pe-K/O/Ana-RLE-Ama-D/E/An-Pep, Pe-K/O/Ana-REL-Ama-D/E/An-Pep, Pe-K/O/Ana-LER-Ama-D/E/An-Pep, Pe-K/O/Ana-ELR-Ama-D/E/An-Pep, Pe-K/O/Ana-DIR-Ama-D/E/An-Pep, Pe-K/O/Ana-IDR-Ama-D/E/An-Pep, Pe-K/O/Ana-RDI-Ama-D/E/An-Pep, Pe-K/O/Ana-RID-Ama-D/E/An-Pep, Pe-K/O/Ana-DLR-Ama-D/E/An-Pep, Pe-K/O/Ana-LDR-Ama-D/E/An-Pep, Pe-K/O/Ana-RDL-Ama-D/E/An-Pep, Pe-K/O/Ana-RLD-Ama-D/E/An-Pep; wherein D/E/An, K/O/Ana and Ama are as defined in claim 137 and/or any other one(s) of the previous claims;

and the compounds:

Pe-K/O/Ana-IRE-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-IRD-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-LRE-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-LRD-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-ERI-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-DRI-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-ERL-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-DRL-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-RIE-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-REI-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-IER-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-EIR-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-RLE-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-REL-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-LER-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-ELR-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-DIR-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-IDR-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-RDI-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-RID-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-DLR-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-LDR-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-RDL-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-RLD-Ama-Ama-D/E/An-Pep; wherein D/E/An, K/O/Ana and Ama are as defined in claim 137 and/or any other one(s) of the previous claims;

and the compounds:

Pe-K/O/Ana-Ama-IRE-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-IRD-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-LRE-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-LRD-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-ERI-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-DRI-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-ERL-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-DRL-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-RIE-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-REI-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-IER-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-EIR-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-RLE-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-REL-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-LER-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-ELR-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-DIR-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-IDR-Ama-D/E/An-Pep, Pe-

K/O/Ana-Ama-RDI-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-RID-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-DLR-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-LDR-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-RDL-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-RLD-Ama-D/E/An-Pep; wherein D/E/An, K/O/Ana and Ama are as defined in claim 137 and/or any other one(s) of the previous claims;

and the compounds:

Pe-K/O/Ana-Ama-IRE-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-IRD-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-LRE-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-LRD-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-ERI-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-DRI-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-ERL-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-DRL-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-RIE-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-REI-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-IER-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-EIR-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-RLE-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-REL-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-LER-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-ELR-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-DIR-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-IDR-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-RDI-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-RID-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-DLR-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-LDR-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-RDL-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-RLD-Ama-Ama-D/E/An-Pep; wherein D/E/An, K/O/Ana and Ama are as defined in claim 137 and/or any other one(s) of the previous claims;

and the compounds:

Pe-K/O/Ana-Ama-Ama-IRE-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-IRD-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-LRE-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-LRD-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-ERI-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-DRI-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-ERL-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-DRL-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-RIE-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-REI-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-IER-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-EIR-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-RLE-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-REL-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-LER-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-ELR-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-DIR-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-IDR-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-RDI-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-RID-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-DLR-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-LDR-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-RDL-Ama-D/E/An-Pep, Pe-K/O/Ana-

Ama-Ama-RLD-Ama-D/E/An-Pep; wherein D/E/An, K/O/Ana and Ama are as defined in claim 137 and/or any other one(s) of the previous claims;

and the compounds:

Pe-K/O/Ana-Ama-Ama-IRE-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-IRD-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-LRE-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-LRD-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-ERI-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-DRI-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-ERL-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-DRL-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-RIE-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-REI-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-IER-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-EIR-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-RLE-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-REL-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-LER-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-ELR-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-DIR-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-IDR-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-RDI-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-RID-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-DLR-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-LDR-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-RDL-Ama-Ama-D/E/An-Pep, Pe-K/O/Ana-Ama-Ama-RLD-Ama-Ama-D/E/An-Pep; wherein D/E/An, K/O/Ana and Ama are as defined in claim 137 and/or any other one(s) of the previous claims;

and the compounds:

Pe-D/E/An-Ama-IRE-K/O/Ana-Pep, Pe-D/E/An-Ama-IRD-K/O/Ana-Pep, Pe-D/E/An-Ama-LRE-K/O/Ana-Pep, Pe-D/E/An-Ama-LRD-K/O/Ana-Pep, Pe-D/E/An-Ama-ERI-K/O/Ana-Pep, Pe-D/E/An-Ama-DRI-K/O/Ana-Pep, Pe-D/E/An-Ama-ERL-K/O/Ana-Pep, Pe-D/E/An-Ama-DRL-K/O/Ana-Pep, Pe-D/E/An-Ama-RIE-K/O/Ana-Pep, Pe-D/E/An-Ama-REI-K/O/Ana-Pep, Pe-D/E/An-Ama-IER-K/O/Ana-Pep, Pe-D/E/An-Ama-EIR-K/O/Ana-Pep, Pe-D/E/An-Ama-RLE-K/O/Ana-Pep, Pe-D/E/An-Ama-REL-K/O/Ana-Pep, Pe-D/E/An-Ama-LER-K/O/Ana-Pep, Pe-D/E/An-Ama-ELR-K/O/Ana-Pep, Pe-D/E/An-Ama-DIR-K/O/Ana-Pep, Pe-D/E/An-Ama-IDR-K/O/Ana-Pep, Pe-D/E/An-Ama-RDI-K/O/Ana-Pep, Pe-D/E/An-Ama-RID-K/O/Ana-Pep, Pe-D/E/An-Ama-DLR-K/O/Ana-Pep, Pe-D/E/An-Ama-LDR-K/O/Ana-Pep, Pe-D/E/An-Ama-RDL-K/O/Ana-Pep, Pe-D/E/An-Ama-RLD-K/O/Ana-Pep; wherein D/E/An, K/O/Ana and Ama are as defined in claim 138 and/or any other one(s) of the previous claims;

and the compounds:

Pe-D/E/An-Ama-Ama-IRE-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-IRD-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-LRE-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-LRD-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-ERI-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-DRI-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-ERL-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-DRL-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-RIE-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-REI-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-IER-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-EIR-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-RLE-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-REL-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-LER-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-ELR-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-DIR-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-IDR-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-RDI-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-RID-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-DLR-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-LDR-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-RDL-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-RLD-K/O/Ana-Pep; wherein D/E/An, K/O/Ana and Ama are as defined in claim 138 and/or any other one(s) of the previous claims;

and the compounds:

Pe-D/E/An-IRE-Ama-K/O/Ana-Pep, Pe-D/E/An-IRD-Ama-K/O/Ana-Pep, Pe-D/E/An-LRE-Ama-K/O/Ana-Pep, Pe-D/E/An-LRD-Ama-K/O/Ana-Pep, Pe-D/E/An-ERI-Ama-K/O/Ana-Pep, Pe-D/E/An-DRI-Ama-K/O/Ana-Pep, Pe-D/E/An-ERL-Ama-K/O/Ana-Pep, Pe-D/E/An-DRL-Ama-K/O/Ana-Pep, Pe-D/E/An-RIE-Ama-K/O/Ana-Pep, Pe-D/E/An-REI-Ama-K/O/Ana-Pep, Pe-D/E/An-IER-Ama-K/O/Ana-Pep, Pe-D/E/An-EIR-Ama-K/O/Ana-Pep, Pe-D/E/An-RLE-Ama-K/O/Ana-Pep, Pe-D/E/An-REL-Ama-K/O/Ana-Pep, Pe-D/E/An-LER-Ama-K/O/Ana-Pep, Pe-D/E/An-ELR-Ama-K/O/Ana-Pep, Pe-D/E/An-DIR-Ama-K/O/Ana-Pep, Pe-D/E/An-IDR-Ama-K/O/Ana-Pep, Pe-D/E/An-RDI-Ama-K/O/Ana-Pep, Pe-D/E/An-RID-Ama-K/O/Ana-Pep, Pe-D/E/An-DLR-Ama-K/O/Ana-Pep, Pe-D/E/An-LDR-Ama-K/O/Ana-Pep, Pe-D/E/An-RDL-Ama-K/O/Ana-Pep, Pe-D/E/An-RLD-Ama-K/O/Ana-Pep; wherein D/E/An, K/O/Ana and Ama are as defined in claim 138 and/or any other one(s) of the previous claims;

and the compounds:

Pe-D/E/An-IRE-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-IRD-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-LRE-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-LRD-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-ERI-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-DRI-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-ERL-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-DRL-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-RIE-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-REI-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-IER-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-EIR-Ama-Ama-K/O/Ana-Pep, Pe-

D/E/An-RLE-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-REL-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-LER-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-ELR-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-DIR-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-IDR-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-RDI-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-RID-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-DLR-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-LDR-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-RDL-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-RLD-Ama-Ama-K/O/Ana-Pep; wherein D/E/An, K/O/Ana and Ama are as defined in claim 138 and/or any other one(s) of the previous claims;

and the compounds:

Pe-D/E/An-Ama-IRE-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-IRD-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-LRE-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-LRD-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-ERI-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-DRI-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-ERL-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-DRL-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-RIE-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-REI-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-IER-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-EIR-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-RLE-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-REL-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-LER-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-ELR-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-DIR-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-IDR-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-RDI-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-RID-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-DLR-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-LDR-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-RDL-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-RLD-Ama-K/O/Ana-Pep; wherein D/E/An, K/O/Ana and Ama are as defined in claim 138 and/or any other one(s) of the previous claims;

and the compounds:

Pe-D/E/An-Ama-IRE-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-IRD-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-LRE-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-LRD-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-ERI-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-DRI-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-ERL-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-DRL-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-RIE-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-REI-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-IER-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-EIR-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-RLE-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-REL-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-LER-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-ELR-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-DIR-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-IDR-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-RDI-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-RID-Ama-Ama-

K/O/Ana-Pep, Pe-D/E/An-Ama-DLR-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-LDR-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-RDL-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-RLD-Ama-Ama-K/O/Ana-Pep; wherein D/E/An, K/O/Ana and Ama are as defined in claim 138 and/or any other one(s) of the previous claims;

and the compounds:

Pe-D/E/An-Ama-Ama-IRE-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-IRD-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-LRE-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-LRD-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-ERI-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-DRI-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-ERL-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-DRL-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-RIE-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-REI-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-IER-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-EIR-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-RLE-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-REL-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-LER-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-ELR-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-DIR-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-IDR-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-RDI-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-RID-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-DLR-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-LDR-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-RDL-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-RLD-Ama-K/O/Ana-Pep; wherein D/E/An, K/O/Ana and Ama are as defined in claim 138 and/or any other one(s) of the previous claims;

and the compounds:

Pe-D/E/An-Ama-Ama-IRE-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-IRD-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-LRE-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-LRD-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-ERI-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-DRI-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-ERL-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-DRL-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-RIE-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-REI-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-IER-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-EIR-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-RLE-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-REL-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-LER-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-ELR-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-DIR-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-IDR-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-RDI-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-RID-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-DLR-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-LDR-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-

Ama-Ama-RDL-Ama-Ama-K/O/Ana-Pep, Pe-D/E/An-Ama-Ama-RLD-Ama-Ama-K/O/Ana-Pep; wherein D/E/An, K/O/Ana and Ama are as defined in claim 138 and/or any other one(s) of the previous claims;

and the compounds:

Pe-K/O/Ana-Peptseq-IRE-D/E/An-Pep, Pe-K/O/Ana-Peptseq-IRD-D/E/An-Pep, Pe-K/O/Ana-Peptseq-LRE-D/E/An-Pep, Pe-K/O/Ana-Peptseq-LRD-D/E/An-Pep, Pe-K/O/Ana-Peptseq-ERI-D/E/An-Pep, Pe-K/O/Ana-Peptseq-DRI-D/E/An-Pep, Pe-K/O/Ana-Peptseq-ERL-D/E/An-Pep, Pe-K/O/Ana-Peptseq-DRL-D/E/An-Pep, Pe-K/O/Ana-Peptseq-RIE-D/E/An-Pep, Pe-K/O/Ana-Peptseq-REI-D/E/An-Pep, Pe-K/O/Ana-Peptseq-IER-D/E/An-Pep, Pe-K/O/Ana-Peptseq-EIR-D/E/An-Pep, Pe-K/O/Ana-Peptseq-RLE-D/E/An-Pep, Pe-K/O/Ana-Peptseq-REL-D/E/An-Pep, Pe-K/O/Ana-Peptseq-LER-D/E/An-Pep, Pe-K/O/Ana-Peptseq-ELR-D/E/An-Pep, Pe-K/O/Ana-Peptseq-DIR-D/E/An-Pep, Pe-K/O/Ana-Peptseq-IDR-D/E/An-Pep, Pe-K/O/Ana-Peptseq-RDI-D/E/An-Pep, Pe-K/O/Ana-Peptseq-RID-D/E/An-Pep, Pe-K/O/Ana-Peptseq-DLR-D/E/An-Pep, Pe-K/O/Ana-Peptseq-LDR-D/E/An-Pep, Pe-K/O/Ana-Peptseq-RDL-D/E/An-Pep, Pe-K/O/Ana-Peptseq-RLD-D/E/An-Pep; wherein D/E/An, K/O/Ana and Peptseq are as defined in claim 139 and/or any other one(s) of the previous claims;

and the compounds:

Pe-K/O/Ana-IRE-Peptseq-D/E/An-Pep, Pe-K/O/Ana-IRD-Peptseq-D/E/An-Pep, Pe-K/O/Ana-LRE-Peptseq-D/E/An-Pep, Pe-K/O/Ana-LRD-Peptseq-D/E/An-Pep, Pe-K/O/Ana-ERI-Peptseq-D/E/An-Pep, Pe-K/O/Ana-DRI-Peptseq-D/E/An-Pep, Pe-K/O/Ana-ERL-Peptseq-D/E/An-Pep, Pe-K/O/Ana-DRL-Peptseq-D/E/An-Pep, Pe-K/O/Ana-RIE-Peptseq-D/E/An-Pep, Pe-K/O/Ana-REI-Peptseq-D/E/An-Pep, Pe-K/O/Ana-IER-Peptseq-D/E/An-Pep, Pe-K/O/Ana-EIR-Peptseq-D/E/An-Pep, Pe-K/O/Ana-RLE-Peptseq-D/E/An-Pep, Pe-K/O/Ana-REL-Peptseq-D/E/An-Pep, Pe-K/O/Ana-LER-Peptseq-D/E/An-Pep, Pe-K/O/Ana-ELR-Peptseq-D/E/An-Pep, Pe-K/O/Ana-DIR-Peptseq-D/E/An-Pep, Pe-K/O/Ana-IDR-Peptseq-D/E/An-Pep, Pe-K/O/Ana-RDI-Peptseq-D/E/An-Pep, Pe-K/O/Ana-RID-Peptseq-D/E/An-Pep, Pe-K/O/Ana-DLR-Peptseq-D/E/An-Pep, Pe-K/O/Ana-LDR-Peptseq-D/E/An-Pep, Pe-K/O/Ana-RDL-Peptseq-D/E/An-Pep, Pe-K/O/Ana-RLD-Peptseq-D/E/An-Pep; wherein D/E/An, K/O/Ana and Peptseq are as defined in claim 139 and/or any other one(s) of the previous claims;

and the compounds:

Pe-K/O/Ana-Peptseq-IRE-Peptseq-D/E/An-Pep, Pe-K/O/Ana-Peptseq-IRD-Peptseq-

D/E/An-Pep, Pe-K/O/Ana-Peptseq-LRE-Peptseq-D/E/An-Pep, Pe-K/O/Ana-Peptseq-LRD-Peptseq-D/E/An-Pep, Pe-K/O/Ana-Peptseq-ERI-Peptseq-D/E/An-Pep, Pe-K/O/Ana-Peptseq-DRI-Peptseq-D/E/An-Pep, Pe-K/O/Ana-Peptseq-ERL-Peptseq-D/E/An-Pep, Pe-K/O/Ana-Peptseq-DRL-Peptseq-D/E/An-Pep, Pe-K/O/Ana-Peptseq-RIE-Peptseq-D/E/An-Pep, Pe-K/O/Ana-Peptseq-REI-Peptseq-D/E/An-Pep, Pe-K/O/Ana-Peptseq-IER-Peptseq-D/E/An-Pep, Pe-K/O/Ana-Peptseq-EIR-Peptseq-D/E/An-Pep, Pe-K/O/Ana-Peptseq-RLE-Peptseq-D/E/An-Pep, Pe-K/O/Ana-Peptseq-REL-Peptseq-D/E/An-Pep, Pe-K/O/Ana-Peptseq-LER-Peptseq-D/E/An-Pep, Pe-K/O/Ana-Peptseq-ELR-Peptseq-D/E/An-Pep, Pe-K/O/Ana-Peptseq-DIR-Peptseq-D/E/An-Pep, Pe-K/O/Ana-Peptseq-IDR-Peptseq-D/E/An-Pep, Pe-K/O/Ana-Peptseq-RDI-Peptseq-D/E/An-Pep, Pe-K/O/Ana-Peptseq-RID-Peptseq-D/E/An-Pep, Pe-K/O/Ana-Peptseq-DLR-Peptseq-D/E/An-Pep, Pe-K/O/Ana-Peptseq-LDR-Peptseq-D/E/An-Pep, Pe-K/O/Ana-Peptseq-RDL-Peptseq-D/E/An-Pep, Pe-K/O/Ana-Peptseq-RLD-Peptseq-D/E/An-Pep; wherein D/E/An, K/O/Ana and Peptseq are as defined in claim 139 and/or any other one(s) of the previous claims;

in any of which optionally:

a disulphide bridge exists between thiol groups, and/or
a disulphide bridge does not exist between thiol groups, and/or
the presence/number of disulphide bridge(s) is undetermined and/or uncertain and/or fluctuating and/or variable and/or subject to change and/or fluctuation and/or uncomplete and/or partial;

and/or in any of which, between K/O/Ana and D/E/An, optionally:

a lactam bridge exists, and/or
a lactam bridge does not exist, and/or
the presence/number of lactam bridge(s) is undetermined and/or uncertain and/or fluctuating and/or variable and/or subject to change and/or fluctuation and/or uncomplete and/or partial;

and wherein Pe and Pep, independently of each other and independently of any other structural unit(s)/part(s), are selected from the group of:

natural amino acids/amino acid residues, and

unnatural amino acids/amino acid residues that comprise maximally 35 non-hydrogen atoms and an unlimited number of hydrogen atoms each, and

peptide sequences/residues comprising 2 to 25, preferably 2 to 10, more preferably 2 to 6, and most preferably 2 to 4, natural amino acids/amino acid residues and/or unnatural amino acids/amino acid residues that each comprise

maximally 35 non-hydrogen atoms and an unlimited number of hydrogen atoms;

and/or: Pe means that the C or K/O/Ana or D/E/An to which Pe is connected by a line (-) in the formula in question is unsubstituted (absence of substituent(s); hydrogen) or Pep means that the C or K/O/Ana or D/E/An to which Pep is connected by a line (-) in the formula in question is unsubstituted (absence of substituent(s); hydrogen);

and wherein any amino acid(s) may comprise L amino acid(s) and/or D amino acid(s) and/or any other optical isomer(s);

and:

- any salt(s)
- any ester(s)
- any amide(s)
- any hydrazide(s)
- any *N*-substituted amide(s)
- any *N*-substituted hydrazide(s)
- any hydroxamic acid derivative(s)
- any decarboxylated analogue(s)
- any *N*-substituted derivative(s)
- any other related derivative(s)
- any other related analogue(s)
- any protected derivative(s) and analogue(s)
- any activated derivative(s) and analogue(s)
- any resin-bound derivative(s) and analogue(s)
- any combination(s) of any of such salt, derivative and/or analogue types

of any of said compounds.

142. The compounds:

Ef-CIREC-Eff, Ef-CIRDC-Eff, Ef-CLREC-Eff, Ef-CLRDC-Eff, Ef-CERIC-Eff, Ef-CDRIC-Eff, Ef-CERLC-Eff, Ef-CDRLC-Eff, Ef-CRIEC-Eff, Ef-CREIC-Eff, Ef-CIERC-Eff, Ef-CEIRC-Eff, Ef-CRLEC-Eff, Ef-CRELC-Eff, Ef-CLERC-Eff, Ef-CELRC-Eff, Ef-CDIRC-Eff, Ef-CIDRC-Eff, Ef-CRDIC-Eff, Ef-CRIDC-Eff, Ef-CDLRC-Eff, Ef-CLDRC-Eff, Ef-CRDLC-Eff and Ef-CRLDC-Eff;

and the compounds:

Ef-D/E/An-IRE-K/O/Ana-Eff, Ef-D/E/An-IRD-K/O/Ana-Eff, Ef-D/E/An-LRE-K/O/Ana-Eff, Ef-D/E/An-LRD-K/O/Ana-Eff, Ef-D/E/An-ERI-K/O/Ana-Eff, Ef-D/E/An-DRI-K/O/Ana-Eff, Ef-D/E/An-ERL-K/O/Ana-Eff, Ef-D/E/An-DRL-K/O/Ana-Eff, Ef-D/E/An-RIE-K/O/Ana-Eff, Ef-D/E/An-REI-K/O/Ana-Eff, Ef-D/E/An-IER-K/O/Ana-Eff, Ef-D/E/An-EIR-K/O/Ana-Eff, Ef-D/E/An-RLE-K/O/Ana-Eff, Ef-D/E/An-REL-K/O/Ana-Eff, Ef-D/E/An-LER-K/O/Ana-Eff, Ef-D/E/An-ELR-K/O/Ana-Eff, Ef-D/E/An-DIR-K/O/Ana-Eff, Ef-D/E/An-IDR-K/O/Ana-Eff, Ef-D/E/An-RDI-K/O/Ana-Eff, Ef-D/E/An-RID-K/O/Ana-Eff, Ef-D/E/An-DLR-K/O/Ana-Eff, Ef-D/E/An-LDR-K/O/Ana-Eff, Ef-D/E/An-RDL-K/O/Ana-Eff, Ef-D/E/An-RLD-K/O/Ana-Eff; wherein D/E/An and K/O/Ana are as defined in claim 135 and/or any other one(s) of the previous claims;

and the compounds:

Ef-K/O/Ana-IRE-D/E/An-Eff, Ef-K/O/Ana-IRD-D/E/An-Eff, Ef-K/O/Ana-LRE-D/E/An-Eff, Ef-K/O/Ana-LRD-D/E/An-Eff, Ef-K/O/Ana-ERI-D/E/An-Eff, Ef-K/O/Ana-DRI-D/E/An-Eff, Ef-K/O/Ana-ERL-D/E/An-Eff, Ef-K/O/Ana-DRL-D/E/An-Eff, Ef-K/O/Ana-RIE-D/E/An-Eff, Ef-K/O/Ana-REI-D/E/An-Eff, Ef-K/O/Ana-IER-D/E/An-Eff, Ef-K/O/Ana-EIR-D/E/An-Eff, Ef-K/O/Ana-RLE-D/E/An-Eff, Ef-K/O/Ana-REL-D/E/An-Eff, Ef-K/O/Ana-LER-D/E/An-Eff, Ef-K/O/Ana-ELR-D/E/An-Eff, Ef-K/O/Ana-DIR-D/E/An-Eff, Ef-K/O/Ana-IDR-D/E/An-Eff, Ef-K/O/Ana-RDI-D/E/An-Eff, Ef-K/O/Ana-RID-D/E/An-Eff, Ef-K/O/Ana-DLR-D/E/An-Eff, Ef-K/O/Ana-LDR-D/E/An-Eff, Ef-K/O/Ana-RDL-D/E/An-Eff, Ef-K/O/Ana-RLD-D/E/An-Eff; wherein D/E/An and K/O/Ana are as defined in claim 136 and/or any other one(s) of the previous claims;

and the compounds:

Ef-K/O/Ana-Ama-IRE-D/E/An-Eff, Ef-K/O/Ana-Ama-IRD-D/E/An-Eff, Ef-K/O/Ana-Ama-LRE-D/E/An-Eff, Ef-K/O/Ana-Ama-LRD-D/E/An-Eff, Ef-K/O/Ana-Ama-ERI-D/E/An-Eff, Ef-K/O/Ana-Ama-DRI-D/E/An-Eff, Ef-K/O/Ana-Ama-ERL-D/E/An-Eff, Ef-K/O/Ana-Ama-DRL-D/E/An-Eff, Ef-K/O/Ana-Ama-RIE-D/E/An-Eff, Ef-K/O/Ana-Ama-REI-D/E/An-Eff, Ef-K/O/Ana-Ama-IER-D/E/An-Eff, Ef-K/O/Ana-Ama-EIR-D/E/An-Eff, Ef-K/O/Ana-Ama-RLE-D/E/An-Eff, Ef-K/O/Ana-Ama-REL-D/E/An-Eff, Ef-K/O/Ana-Ama-LER-D/E/An-Eff, Ef-K/O/Ana-Ama-ELR-D/E/An-Eff, Ef-K/O/Ana-Ama-DIR-D/E/An-Eff, Ef-K/O/Ana-Ama-IDR-D/E/An-Eff, Ef-K/O/Ana-Ama-RDI-D/E/An-Eff, Ef-K/O/Ana-Ama-RID-D/E/An-Eff, Ef-K/O/Ana-Ama-DLR-D/E/An-Eff, Ef-K/O/Ana-Ama-LDR-D/E/An-Eff, Ef-K/O/Ana-Ama-RDL-D/E/An-Eff, Ef-K/O/Ana-Ama-RLD-D/E/An-Eff; wherein D/E/An, K/O/Ana and Ama are as defined in claim 137 and/or any other one(s) of the previous claims;

and the compounds:

Ef-K/O/Ana-Ama-Ama-IRE-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-IRD-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-LRE-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-LRD-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-ERI-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-DRI-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-ERL-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-DRL-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-RIE-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-REI-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-IER-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-EIR-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-RLE-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-REL-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-LER-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-ELR-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-DIR-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-IDR-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-RDI-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-RID-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-DLR-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-LDR-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-RDL-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-RLD-D/E/An-Eff; wherein D/E/An, K/O/Ana and Ama are as defined in claim 137 and/or any other one(s) of the previous claims;

and the compounds:

Ef-K/O/Ana-IRE-Ama-D/E/An-Eff, Ef-K/O/Ana-IRD-Ama-D/E/An-Eff, Ef-K/O/Ana-LRE-Ama-D/E/An-Eff, Ef-K/O/Ana-LRD-Ama-D/E/An-Eff, Ef-K/O/Ana-ERI-Ama-D/E/An-Eff, Ef-K/O/Ana-DRI-Ama-D/E/An-Eff, Ef-K/O/Ana-ERL-Ama-D/E/An-Eff, Ef-K/O/Ana-DRL-Ama-D/E/An-Eff, Ef-K/O/Ana-RIE-Ama-D/E/An-Eff, Ef-K/O/Ana-REI-Ama-D/E/An-Eff, Ef-K/O/Ana-IER-Ama-D/E/An-Eff, Ef-K/O/Ana-EIR-Ama-D/E/An-Eff, Ef-K/O/Ana-RLE-Ama-D/E/An-Eff, Ef-K/O/Ana-REL-Ama-D/E/An-Eff, Ef-K/O/Ana-LER-Ama-D/E/An-Eff, Ef-K/O/Ana-ELR-Ama-D/E/An-Eff, Ef-K/O/Ana-DIR-Ama-D/E/An-Eff, Ef-K/O/Ana-IDR-Ama-D/E/An-Eff, Ef-K/O/Ana-RDI-Ama-D/E/An-Eff, Ef-K/O/Ana-RID-Ama-D/E/An-Eff, Ef-K/O/Ana-DLR-Ama-D/E/An-Eff, Ef-K/O/Ana-LDR-Ama-D/E/An-Eff, Ef-K/O/Ana-RDL-Ama-D/E/An-Eff, Ef-K/O/Ana-RLD-Ama-D/E/An-Eff; wherein D/E/An, K/O/Ana and Ama are as defined in claim 137 and/or any other one(s) of the previous claims;

and the compounds:

Ef-K/O/Ana-IRE-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-IRD-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-LRE-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-LRD-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-ERI-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-DRI-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-ERL-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-DRL-Ama-Ama-D/E/An-Eff, Ef-

K/O/Ana-RIE-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-REI-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-IER-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-EIR-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-RLE-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-REL-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-LER-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-ELR-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-DIR-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-IDR-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-RDI-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-RID-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-DLR-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-LDR-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-RDL-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-RLD-Ama-Ama-D/E/An-Eff; wherein D/E/An, K/O/Ana and Ama are as defined in claim 137 and/or any other one(s) of the previous claims;

and the compounds:

Ef-K/O/Ana-Ama-IRE-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-IRD-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-LRE-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-LRD-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-ERI-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-DRI-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-ERL-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-DRL-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-RIE-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-REI-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-IER-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-EIR-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-RLE-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-REL-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-LER-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-ELR-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-DIR-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-IDR-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-RDI-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-RID-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-DLR-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-LDR-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-RDL-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-RLD-Ama-D/E/An-Eff; wherein D/E/An, K/O/Ana and Ama are as defined in claim 137 and/or any other one(s) of the previous claims;

and the compounds:

Ef-K/O/Ana-Ama-IRE-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-IRD-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-LRE-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-LRD-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-ERI-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-DRI-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-ERL-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-DRL-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-RIE-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-REI-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-IER-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-EIR-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-RLE-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-REL-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-LER-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-ELR-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-

Ama-DIR-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-IDR-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-RDI-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-RID-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-DLR-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-LDR-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-RDL-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-RLD-Ama-Ama-D/E/An-Eff; wherein D/E/An, K/O/Ana and Ama are as defined in claim 137 and/or any other one(s) of the previous claims;

and the compounds:

Ef-K/O/Ana-Ama-Ama-IRE-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-IRD-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-LRE-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-LRD-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-ERI-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-DRI-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-ERL-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-DRL-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-RIE-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-REI-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-IER-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-EIR-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-RLE-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-REL-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-LER-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-ELR-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-DIR-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-IDR-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-RDI-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-RID-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-DLR-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-LDR-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-RDL-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-RLD-Ama-D/E/An-Eff; wherein D/E/An, K/O/Ana and Ama are as defined in claim 137 and/or any other one(s) of the previous claims;

and the compounds:

Ef-K/O/Ana-Ama-Ama-IRE-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-IRD-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-LRE-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-LRD-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-ERI-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-DRI-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-ERL-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-DRL-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-RIE-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-REI-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-IER-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-EIR-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-RLE-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-REL-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-LER-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-ELR-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-DIR-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-IDR-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-RDI-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-RID-

Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-DLR-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-LDR-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-RDL-Ama-Ama-D/E/An-Eff, Ef-K/O/Ana-Ama-Ama-RLD-Ama-Ama-D/E/An-Eff; wherein D/E/An, K/O/Ana and Ama are as defined in claim 137 and/or any other one(s) of the previous claims;

and the compounds:

Ef-D/E/An-Ama-IRE-K/O/Ana-Eff, Ef-D/E/An-Ama-IRD-K/O/Ana-Eff, Ef-D/E/An-Ama-LRE-K/O/Ana-Eff, Ef-D/E/An-Ama-LRD-K/O/Ana-Eff, Ef-D/E/An-Ama-ERI-K/O/Ana-Eff, Ef-D/E/An-Ama-DRI-K/O/Ana-Eff, Ef-D/E/An-Ama-ERL-K/O/Ana-Eff, Ef-D/E/An-Ama-DRL-K/O/Ana-Eff, Ef-D/E/An-Ama-RIE-K/O/Ana-Eff, Ef-D/E/An-Ama-REI-K/O/Ana-Eff, Ef-D/E/An-Ama-IER-K/O/Ana-Eff, Ef-D/E/An-Ama-EIR-K/O/Ana-Eff, Ef-D/E/An-Ama-RLE-K/O/Ana-Eff, Ef-D/E/An-Ama-REL-K/O/Ana-Eff, Ef-D/E/An-Ama-LER-K/O/Ana-Eff, Ef-D/E/An-Ama-ELR-K/O/Ana-Eff, Ef-D/E/An-Ama-DIR-K/O/Ana-Eff, Ef-D/E/An-Ama-IDR-K/O/Ana-Eff, Ef-D/E/An-Ama-RDI-K/O/Ana-Eff, Ef-D/E/An-Ama-RID-K/O/Ana-Eff, Ef-D/E/An-Ama-DLR-K/O/Ana-Eff, Ef-D/E/An-Ama-LDR-K/O/Ana-Eff, Ef-D/E/An-Ama-RDL-K/O/Ana-Eff, Ef-D/E/An-Ama-RLD-K/O/Ana-Eff; wherein D/E/An, K/O/Ana and Ama are as defined in claim 138 and/or any other one(s) of the previous claims;

and the compounds:

Ef-D/E/An-Ama-Ama-IRE-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-IRD-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-LRE-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-LRD-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-ERI-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-DRI-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-ERL-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-DRL-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-RIE-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-REI-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-IER-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-EIR-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-RLE-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-REL-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-LER-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-ELR-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-DIR-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-IDR-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-RDI-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-RID-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-DLR-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-LDR-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-RDL-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-RLD-K/O/Ana-Eff; wherein D/E/An, K/O/Ana and Ama are as defined in claim 138 and/or any other one(s) of the previous claims;

and the compounds:

Ef-D/E/An-IRE-Ama-K/O/Ana-Eff, Ef-D/E/An-IRD-Ama-K/O/Ana-Eff, Ef-D/E/An-LRE-Ama-K/O/Ana-Eff, Ef-D/E/An-LRD-Ama-K/O/Ana-Eff, Ef-D/E/An-ERI-Ama-K/O/Ana-Eff, Ef-D/E/An-DRI-Ama-K/O/Ana-Eff, Ef-D/E/An-ERL-Ama-K/O/Ana-Eff, Ef-D/E/An-DRL-Ama-K/O/Ana-Eff, Ef-D/E/An-RIE-Ama-K/O/Ana-Eff, Ef-D/E/An-REI-Ama-K/O/Ana-Eff, Ef-D/E/An-IER-Ama-K/O/Ana-Eff, Ef-D/E/An-EIR-Ama-K/O/Ana-Eff, Ef-D/E/An-RLE-Ama-K/O/Ana-Eff, Ef-D/E/An-REL-Ama-K/O/Ana-Eff, Ef-D/E/An-LER-Ama-K/O/Ana-Eff, Ef-D/E/An-ELR-Ama-K/O/Ana-Eff, Ef-D/E/An-DIR-Ama-K/O/Ana-Eff, Ef-D/E/An-IDR-Ama-K/O/Ana-Eff, Ef-D/E/An-RDI-Ama-K/O/Ana-Eff, Ef-D/E/An-RID-Ama-K/O/Ana-Eff, Ef-D/E/An-DLR-Ama-K/O/Ana-Eff, Ef-D/E/An-LDR-Ama-K/O/Ana-Eff, Ef-D/E/An-RDL-Ama-K/O/Ana-Eff, Ef-D/E/An-RLD-Ama-K/O/Ana-Eff; wherein D/E/An, K/O/Ana and Ama are as defined in claim 138 and/or any other one(s) of the previous claims;

and the compounds:

Ef-D/E/An-IRE-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-IRD-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-LRE-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-LRD-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-ERI-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-DRI-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-ERL-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-DRL-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-RIE-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-REI-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-IER-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-EIR-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-RLE-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-REL-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-LER-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-ELR-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-DIR-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-IDR-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-RDI-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-RID-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-DLR-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-LDR-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-RDL-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-RLD-Ama-Ama-K/O/Ana-Eff; wherein D/E/An, K/O/Ana and Ama are as defined in claim 138 and/or any other one(s) of the previous claims;

and the compounds:

Ef-D/E/An-Ama-IRE-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-IRD-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-LRE-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-LRD-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-ERI-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-DRI-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-ERL-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-DRL-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-RIE-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-REI-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-IER-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-EIR-Ama-K/O/Ana-Eff, Ef-

D/E/An-Ama-RLE-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-REL-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-LER-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-ELR-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-DIR-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-IDR-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-RDI-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-RID-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-DLR-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-LDR-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-RDL-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-RLD-Ama-K/O/Ana-Eff; wherein D/E/An, K/O/Ana and Ama are as defined in claim 138 and/or any other one(s) of the previous claims;

and the compounds:

Ef-D/E/An-Ama-IRE-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-IRD-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-LRE-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-LRD-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-ERI-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-DRI-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-ERL-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-DRL-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-RIE-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-REI-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-IER-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-EIR-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-RLE-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-REL-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-LER-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-ELR-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-DIR-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-IDR-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-RDI-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-RID-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-DLR-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-LDR-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-RDL-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-RLD-Ama-Ama-K/O/Ana-Eff; wherein D/E/An, K/O/Ana and Ama are as defined in claim 138 and/or any other one(s) of the previous claims;

and the compounds:

Ef-D/E/An-Ama-Ama-IRE-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-IRD-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-LRE-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-LRD-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-ERI-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-DRI-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-ERL-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-DRL-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-RIE-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-REI-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-IER-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-EIR-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-RLE-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-REL-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-LER-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-ELR-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-DIR-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-IDR-Ama-K/O/Ana-Eff, Ef-

D/E/An-Ama-Ama-RDI-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-RID-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-DLR-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-LDR-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-RDL-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-RLD-Ama-K/O/Ana-Eff; wherein D/E/An, K/O/Ana and Ama are as defined in claim 138 and/or any other one(s) of the previous claims;

and the compounds:

Ef-D/E/An-Ama-Ama-IRE-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-IRD-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-LRE-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-LRD-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-ERI-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-DRI-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-ERL-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-DRL-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-RIE-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-REI-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-IER-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-EIR-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-RLE-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-REL-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-LER-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-ELR-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-DIR-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-IDR-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-RDI-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-RID-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-DLR-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-LDR-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-RDL-Ama-Ama-K/O/Ana-Eff, Ef-D/E/An-Ama-Ama-RLD-Ama-Ama-K/O/Ana-Eff; wherein D/E/An, K/O/Ana and Ama are as defined in claim 138 and/or any other one(s) of the previous claims;

and the compounds:

Ef-K/O/Ana-Peptseq-IRE-D/E/An-Eff, Ef-K/O/Ana-Peptseq-IRD-D/E/An-Eff, Ef-K/O/Ana-Peptseq-LRE-D/E/An-Eff, Ef-K/O/Ana-Peptseq-LRD-D/E/An-Eff, Ef-K/O/Ana-Peptseq-ERI-D/E/An-Eff, Ef-K/O/Ana-Peptseq-DRI-D/E/An-Eff, Ef-K/O/Ana-Peptseq-ERL-D/E/An-Eff, Ef-K/O/Ana-Peptseq-DRL-D/E/An-Eff, Ef-K/O/Ana-Peptseq-RIE-D/E/An-Eff, Ef-K/O/Ana-Peptseq-REI-D/E/An-Eff, Ef-K/O/Ana-Peptseq-IER-D/E/An-Eff, Ef-K/O/Ana-Peptseq-EIR-D/E/An-Eff, Ef-K/O/Ana-Peptseq-RLE-D/E/An-Eff, Ef-K/O/Ana-Peptseq-REL-D/E/An-Eff, Ef-K/O/Ana-Peptseq-LER-D/E/An-Eff, Ef-K/O/Ana-Peptseq-ELR-D/E/An-Eff, Ef-K/O/Ana-Peptseq-DIR-D/E/An-Eff, Ef-K/O/Ana-Peptseq-IDR-D/E/An-Eff, Ef-K/O/Ana-Peptseq-RDI-D/E/An-Eff, Ef-K/O/Ana-Peptseq-RID-D/E/An-Eff, Ef-K/O/Ana-Peptseq-DLR-D/E/An-Eff, Ef-K/O/Ana-Peptseq-LDR-D/E/An-Eff, Ef-K/O/Ana-Peptseq-RDL-D/E/An-Eff, Ef-K/O/Ana-Peptseq-RLD-D/E/An-Eff;

wherein D/E/An, K/O/Ana and Peptseq are as defined in claim 139 and/or any other one(s) of the previous claims;

and the compounds:

Ef-K/O/Ana-IRE-Peptseq-D/E/An-Eff, Ef-K/O/Ana-IRD-Peptseq-D/E/An-Eff, Ef-K/O/Ana-LRE-Peptseq-D/E/An-Eff, Ef-K/O/Ana-LRD-Peptseq-D/E/An-Eff, Ef-K/O/Ana-ERI-Peptseq-D/E/An-Eff, Ef-K/O/Ana-DRI-Peptseq-D/E/An-Eff, Ef-K/O/Ana-ERL-Peptseq-D/E/An-Eff, Ef-K/O/Ana-DRL-Peptseq-D/E/An-Eff, Ef-K/O/Ana-RIE-Peptseq-D/E/An-Eff, Ef-K/O/Ana-REI-Peptseq-D/E/An-Eff, Ef-K/O/Ana-IER-Peptseq-D/E/An-Eff, Ef-K/O/Ana-EIR-Peptseq-D/E/An-Eff, Ef-K/O/Ana-RLE-Peptseq-D/E/An-Eff, Ef-K/O/Ana-REL-Peptseq-D/E/An-Eff, Ef-K/O/Ana-LER-Peptseq-D/E/An-Eff, Ef-K/O/Ana-ELR-Peptseq-D/E/An-Eff, Ef-K/O/Ana-DIR-Peptseq-D/E/An-Eff, Ef-K/O/Ana-IDR-Peptseq-D/E/An-Eff, Ef-K/O/Ana-RDI-Peptseq-D/E/An-Eff, Ef-K/O/Ana-RID-Peptseq-D/E/An-Eff, Ef-K/O/Ana-DLR-Peptseq-D/E/An-Eff, Ef-K/O/Ana-LDR-Peptseq-D/E/An-Eff, Ef-K/O/Ana-RDL-Peptseq-D/E/An-Eff, Ef-K/O/Ana-RLD-Peptseq-D/E/An-Eff; wherein D/E/An, K/O/Ana and Peptseq are as defined in claim 139 and/or any other one(s) of the previous claims;

and the compounds:

Ef-K/O/Ana-Peptseq-IRE-Peptseq-D/E/An-Eff, Ef-K/O/Ana-Peptseq-IRD-Peptseq-D/E/An-Eff, Ef-K/O/Ana-Peptseq-LRE-Peptseq-D/E/An-Eff, Ef-K/O/Ana-Peptseq-LRD-Peptseq-D/E/An-Eff, Ef-K/O/Ana-Peptseq-ERI-Peptseq-D/E/An-Eff, Ef-K/O/Ana-Peptseq-DRI-Peptseq-D/E/An-Eff, Ef-K/O/Ana-Peptseq-ERL-Peptseq-D/E/An-Eff, Ef-K/O/Ana-Peptseq-DRL-Peptseq-D/E/An-Eff, Ef-K/O/Ana-Peptseq-RIE-Peptseq-D/E/An-Eff, Ef-K/O/Ana-Peptseq-REI-Peptseq-D/E/An-Eff, Ef-K/O/Ana-Peptseq-IER-Peptseq-D/E/An-Eff, Ef-K/O/Ana-Peptseq-EIR-Peptseq-D/E/An-Eff, Ef-K/O/Ana-Peptseq-RLE-Peptseq-D/E/An-Eff, Ef-K/O/Ana-Peptseq-REL-Peptseq-D/E/An-Eff, Ef-K/O/Ana-Peptseq-LER-Peptseq-D/E/An-Eff, Ef-K/O/Ana-Peptseq-ELR-Peptseq-D/E/An-Eff, Ef-K/O/Ana-Peptseq-DIR-Peptseq-D/E/An-Eff, Ef-K/O/Ana-Peptseq-IDR-Peptseq-D/E/An-Eff, Ef-K/O/Ana-Peptseq-RDI-Peptseq-D/E/An-Eff, Ef-K/O/Ana-Peptseq-RID-Peptseq-D/E/An-Eff, Ef-K/O/Ana-Peptseq-DLR-Peptseq-D/E/An-Eff, Ef-K/O/Ana-Peptseq-LDR-Peptseq-D/E/An-Eff, Ef-K/O/Ana-Peptseq-RDL-Peptseq-D/E/An-Eff, Ef-K/O/Ana-Peptseq-RLD-Peptseq-D/E/An-Eff; wherein D/E/An, K/O/Ana and Peptseq are as defined in claim 139 and/or any other one(s) of the previous claims;

and the compounds:

Ef-D/E/An-Peptseq-IRE-K/O/Ana-Eff, Ef-D/E/An-Peptseq-IRD-K/O/Ana-Eff, Ef-D/E/An-Peptseq-LRE-K/O/Ana-Eff, Ef-D/E/An-Peptseq-LRD-K/O/Ana-Eff, Ef-D/E/An-Peptseq-ERI-K/O/Ana-Eff, Ef-D/E/An-Peptseq-DRI-K/O/Ana-Eff, Ef-D/E/An-Peptseq-ERL-K/O/Ana-Eff, Ef-D/E/An-Peptseq-DRL-K/O/Ana-Eff, Ef-D/E/An-Peptseq-RIE-K/O/Ana-Eff, Ef-D/E/An-Peptseq-REI-K/O/Ana-Eff, Ef-D/E/An-Peptseq-IER-K/O/Ana-Eff, Ef-D/E/An-Peptseq-EIR-K/O/Ana-Eff, Ef-D/E/An-Peptseq-RLE-K/O/Ana-Eff, Ef-D/E/An-Peptseq-REL-K/O/Ana-Eff, Ef-D/E/An-Peptseq-LER-K/O/Ana-Eff, Ef-D/E/An-Peptseq-ELR-K/O/Ana-Eff, Ef-D/E/An-Peptseq-DIR-K/O/Ana-Eff, Ef-D/E/An-Peptseq-IDR-K/O/Ana-Eff, Ef-D/E/An-Peptseq-RDI-K/O/Ana-Eff, Ef-D/E/An-Peptseq-RID-K/O/Ana-Eff, Ef-D/E/An-Peptseq-DLR-K/O/Ana-Eff, Ef-D/E/An-Peptseq-LDR-K/O/Ana-Eff, Ef-D/E/An-Peptseq-RDL-K/O/Ana-Eff, Ef-D/E/An-Peptseq-RLD-K/O/Ana-Eff; wherein K/O/Ana, D/E/An and Peptseq are as defined in claim 139 and/or any other one(s) ef the previous claims;

and the compounds:

Ef-D/E/An-IRE-Peptseq-K/O/Ana-Eff, Ef-D/E/An-IRD-Peptseq-K/O/Ana-Eff, Ef-D/E/An-LRE-Peptseq-K/O/Ana-Eff, Ef-D/E/An-LRD-Peptseq-K/O/Ana-Eff, Ef-D/E/An-ERI-Peptseq-K/O/Ana-Eff, Ef-D/E/An-DRI-Peptseq-K/O/Ana-Eff, Ef-D/E/An-ERL-Peptseq-K/O/Ana-Eff, Ef-D/E/An-DRL-Peptseq-K/O/Ana-Eff, Ef-D/E/An-RIE-Peptseq-K/O/Ana-Eff, Ef-D/E/An-REI-Peptseq-K/O/Ana-Eff, Ef-D/E/An-IER-Peptseq-K/O/Ana-Eff, Ef-D/E/An-EIR-Peptseq-K/O/Ana-Eff, Ef-D/E/An-RLE-Peptseq-K/O/Ana-Eff, Ef-D/E/An-REL-Peptseq-K/O/Ana-Eff, Ef-D/E/An-LER-Peptseq-K/O/Ana-Eff, Ef-D/E/An-ELR-Peptseq-K/O/Ana-Eff, Ef-D/E/An-DIR-Peptseq-K/O/Ana-Eff, Ef-D/E/An-IDR-Peptseq-K/O/Ana-Eff, Ef-D/E/An-RDI-Peptseq-K/O/Ana-Eff, Ef-D/E/An-RID-Peptseq-K/O/Ana-Eff, Ef-D/E/An-DLR-Peptseq-K/O/Ana-Eff, Ef-D/E/An-LDR-Peptseq-K/O/Ana-Eff, Ef-D/E/An-RDL-Peptseq-K/O/Ana-Eff, Ef-D/E/An-RLD-Peptseq-K/O/Ana-Eff; wherein K/O/Ana, D/E/An and Peptseq are as defined in claim 139 and/or any other one(s) of the previous claims;

and the compounds:

Ef-D/E/An-Peptseq-IRE-Peptseq-K/O/Ana-Eff, Ef-D/E/An-Peptseq-IRD-Peptseq-K/O/Ana-Eff, Ef-D/E/An-Peptseq-LRE-Peptseq-K/O/Ana-Eff, Ef-D/E/An-Peptseq-LRD-Peptseq-K/O/Ana-Eff, Ef-D/E/An-Peptseq-ERI-Peptseq-K/O/Ana-Eff, Ef-D/E/An-Peptseq-DRI-Peptseq-K/O/Ana-Eff, Ef-D/E/An-Peptseq-ERL-Peptseq-K/O/Ana-Eff, Ef-D/E/An-Peptseq-DRL-Peptseq-K/O/Ana-Eff, Ef-D/E/An-Peptseq-RIE-Peptseq-K/O/Ana-Eff, Ef-D/E/An-Peptseq-REI-Peptseq-K/O/Ana-Eff, Ef-D/E/An-Peptseq-IER-Peptseq-K/O/Ana-Eff, Ef-D/E/An-Peptseq-EIR-Peptseq-K/O/Ana-Eff, Ef-D/E/An-Peptseq-RLE-

Peptseq-K/O/Ana-Eff, Ef-D/E/An-Peptseq-REL-Peptseq-K/O/Ana-Eff, Ef-D/E/An-Peptseq-LER-Peptseq-K/O/Ana-Eff, Ef-D/E/An-Peptseq-ELR-Peptseq-K/O/Ana-Eff, Ef-D/E/An-Peptseq-DIR-Peptseq-K/O/Ana-Eff, Ef-D/E/An-Peptseq-IDR-Peptseq-K/O/Ana-Eff, Ef-D/E/An-Peptseq-RDI-Peptseq-K/O/Ana-Eff, Ef-D/E/An-Peptseq-RID-Peptseq-K/O/Ana-Eff, Ef-D/E/An-Peptseq-DLR-Peptseq-K/O/Ana-Eff, Ef-D/E/An-Peptseq-LDR-Peptseq-K/O/Ana-Eff, Ef-D/E/An-Peptseq-RDL-Peptseq-K/O/Ana-Eff, Ef-D/E/An-Peptseq-RLD-Peptseq-K/O/Ana-Eff; wherein K/O/Ana, D/E/An and Peptseq are as defined in claim 139 and/or any other one(s) of the previous claims;

in any of which optionally:

a disulphide bridge exists between thiol groups, and/or
a disulphide bridge does not exist between thiol groups, and/or
the presence/number of disulphide bridge(s) is undetermined and/or uncertain and/or fluctuating and/or variable and/or subject to change and/or fluctuation and/or uncomplete and/or partial;

and/or in any of which, between K/O/Ana and D/E/An, optionally:

a lactam bridge exists, and/or
a lactam bridge does not exist, and/or
the presence/number of lactam bridge(s) is undetermined and/or uncertain and/or fluctuating and/or variable and/or subject to change and/or fluctuation and/or uncomplete and/or partial;

and wherein Ef and Eff, independently, are selected from the group of:

effector units, linker units, solubility modifier units, stabilizer units, charge modifier units, spacer units, lysis and/or reaction and/or reactivity modifier units, internalizing and/or internalization enhancer and/or membrane interaction units and/or other local route and/or local attachment/local binding and/or distribution affecting units, adsorption enhancer units, and other related units, and

structures comprising one or more such unit(s);

and wherein any amino acid(s) may comprise L amino acid(s) and/or D amino acid(s) and/or any other optical isomer(s);

and:

- any salt(s)

- any ester(s)
- any amide(s)
- any hydrazide(s)
- any *N*-substituted amide(s)
- any *N*-substituted hydrazide(s)
- any hydroxamic acid derivative(s)
- any decarboxylated analogue(s)
- any *N*-substituted derivative(s)
- any other related derivative(s)
- any other related analogue(s)
- any protected derivative(s) and analogue(s)
- any activated derivative(s) and analogue(s)
- any resin-bound derivative(s) and analogue(s)
- any combination(s) of any of such salt, derivative and/or analogue types

of any of said compounds.

143. The compounds:

CIREC, CIRDC, CLREC, CLRDC, CERIC, CDRIC, CERLC, CDRLC, CRIEC, CREIC, CIERC, CEIRC, CRLEC, CRELC, CLERC, CELRC, CDIRC, CIDRC, CRDIC, CRIDC, CDLRC, CLDRC, CRDLC, CRLDC;

and the compounds:

C/Hcy/Alog-IRE-C/Hcy/Alog, C/Hcy/Alog-IRD-C/Hcy/Alog, C/Hcy/Alog-LRE-C/Hcy/Alog, C/Hcy/Alog-LRD-C/Hcy/Alog, C/Hcy/Alog-ERI-C/Hcy/Alog, C/Hcy/Alog-DRI-C/Hcy/Alog, C/Hcy/Alog-ERL-C/Hcy/Alog, C/Hcy/Alog-DRL-C/Hcy/Alog, C/Hcy/Alog-RIE-C/Hcy/Alog, C/Hcy/Alog-REI-C/Hcy/Alog, C/Hcy/Alog-IER-C/Hcy/Alog, C/Hcy/Alog-EIR-C/Hcy/Alog, C/Hcy/Alog-RLE-C/Hcy/Alog, C/Hcy/Alog-REL-C/Hcy/Alog, C/Hcy/Alog-LER-C/Hcy/Alog, C/Hcy/Alog-ELR-C/Hcy/Alog, C/Hcy/Alog-DIR-C/Hcy/Alog, C/Hcy/Alog-IDR-C/Hcy/Alog, C/Hcy/Alog-RDI-C/Hcy/Alog, C/Hcy/Alog-RID-C/Hcy/Alog, C/Hcy/Alog-DLR-C/Hcy/Alog, C/Hcy/Alog-LDR-C/Hcy/Alog, C/Hcy/Alog-RDL-C/Hcy/Alog, C/Hcy/Alog-RLD-C/Hcy/Alog;

and the compounds:

C/Hcy/Alog-Ama-IRE-C/Hcy/Alog, C/Hcy/Alog-Ama-IRD-C/Hcy/Alog, C/Hcy/Alog-Ama-LRE-C/Hcy/Alog, C/Hcy/Alog-Ama-LRD-C/Hcy/Alog, C/Hcy/Alog-Ama-ERI-

C/Hcy/Alog, C/Hcy/Alog-Ama-DRI-C/Hcy/Alog, C/Hcy/Alog-Ama-ERL-C/Hcy/Alog, C/Hcy/Alog-Ama-DRL-C/Hcy/Alog, C/Hcy/Alog-Ama-RIE-C/Hcy/Alog, C/Hcy/Alog-Ama-REI-C/Hcy/Alog, C/Hcy/Alog-Ama-IER-C/Hcy/Alog, C/Hcy/Alog-Ama-EIR-C/Hcy/Alog, C/Hcy/Alog-Ama-RLE-C/Hcy/Alog, C/Hcy/Alog-Ama-REL-C/Hcy/Alog, C/Hcy/Alog-Ama-LER-C/Hcy/Alog, C/Hcy/Alog-Ama-ELR-C/Hcy/Alog, C/Hcy/Alog-Ama-DIR-C/Hcy/Alog, C/Hcy/Alog-Ama-IDR-C/Hcy/Alog, C/Hcy/Alog-Ama-RDI-C/Hcy/Alog, C/Hcy/Alog-Ama-RID-C/Hcy/Alog, C/Hcy/Alog-Ama-DLR-C/Hcy/Alog, C/Hcy/Alog-Ama-LDR-C/Hcy/Alog, C/Hcy/Alog-Ama-RDL-C/Hcy/Alog, C/Hcy/Alog-Ama-RLD-C/Hcy/Alog;

and the compounds:

C/Hcy/Alog-Ama-Ama-IRE-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-IRD-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-LRE-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-LRD-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-ERI-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-DRI-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-ERL-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-DRL-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-RIE-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-REI-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-IER-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-EIR-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-RLE-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-REL-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-LER-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-ELR-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-DIR-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-IDR-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-RDI-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-RID-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-DLR-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-LDR-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-RDL-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-RLD-C/Hcy/Alog;

and the compounds:

C/Hcy/Alog-Ama-Ama-IRE-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-IRD-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-LRE-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-LRD-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-ERI-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-DRI-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-ERL-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-DRL-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-RIE-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-REI-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-IER-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-EIR-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-RLE-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-REL-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-LER-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-ELR-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-DIR-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-IDR-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-RDI-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-RID-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-DLR-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-

Ama-LDR-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-RDL-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-RLD-Ama-C/Hcy/Alog;

and the compounds:

C/Hcy/Alog-Ama-Ama-IRE-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-IRD-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-LRE-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-LRD-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-ERI-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-DRI-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-ERL-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-DRL-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-RIE-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-REI-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-IER-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-EIR-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-RLE-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-REL-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-LER-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-ELR-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-DIR-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-IDR-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-RDI-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-RID-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-DLR-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-LDR-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-RDL-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-Ama-RLD-Ama-Ama-C/Hcy/Alog;

and the compounds:

C/Hcy/Alog-IRE-Ama-C/Hcy/Alog, C/Hcy/Alog-IRD-Ama-C/Hcy/Alog, C/Hcy/Alog-LRE-Ama-C/Hcy/Alog, C/Hcy/Alog-LRD-Ama-C/Hcy/Alog, C/Hcy/Alog-ERI-Ama-C/Hcy/Alog, C/Hcy/Alog-DRI-Ama-C/Hcy/Alog, C/Hcy/Alog-ERL-Ama-C/Hcy/Alog, C/Hcy/Alog-DRL-Ama-C/Hcy/Alog, C/Hcy/Alog-RIE-Ama-C/Hcy/Alog, C/Hcy/Alog-REI-Ama-C/Hcy/Alog, C/Hcy/Alog-IER-Ama-C/Hcy/Alog, C/Hcy/Alog-EIR-Ama-C/Hcy/Alog, C/Hcy/Alog-RLE-Ama-C/Hcy/Alog, C/Hcy/Alog-REL-Ama-C/Hcy/Alog, C/Hcy/Alog-LER-Ama-C/Hcy/Alog, C/Hcy/Alog-ELR-Ama-C/Hcy/Alog, C/Hcy/Alog-DIR-Ama-C/Hcy/Alog, C/Hcy/Alog-IDR-Ama-C/Hcy/Alog, C/Hcy/Alog-RDI-Ama-C/Hcy/Alog, C/Hcy/Alog-RID-Ama-C/Hcy/Alog, C/Hcy/Alog-DLR-Ama-C/Hcy/Alog, C/Hcy/Alog-LDR-Ama-C/Hcy/Alog, C/Hcy/Alog-RDL-Ama-C/Hcy/Alog, C/Hcy/Alog-RLD-Ama-C/Hcy/Alog;

and the compounds:

C/Hcy/Alog-IRE-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-IRD-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-LRE-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-LRD-Ama-Ama-C/Hcy/Alog,

C/Hcy/Alog-ERI-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-DRI-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-ERL-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-DRL-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-RIE-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-REI-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-IER-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-EIR-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-RLE-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-REL-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-LER-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-ELR-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-DIR-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-IDR-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-RDI-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-RID-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-DLR-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-LDR-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-RDL-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-RLD-Ama-Ama-C/Hcy/Alog;

and the compounds:

C/Hcy/Alog-Ama-IRE-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-IRD-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-LRE-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-LRD-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-ERI-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-DRI-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-ERL-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-DRL-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-RIE-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-REI-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-IER-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-EIR-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-RLE-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-REL-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-LER-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-ELR-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-DIR-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-IDR-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-RDI-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-RID-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-DLR-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-LDR-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-RDL-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-RLD-Ama-C/Hcy/Alog;

and the compounds:

C/Hcy/Alog-Ama-IRE-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-IRD-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-LRE-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-LRD-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-ERI-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-DRI-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-ERL-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-DRL-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-RIE-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-REI-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-IER-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-EIR-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-RLE-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-REL-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-LER-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-ELR-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-DIR-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-IDR-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-RDI-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-RID-Ama-

Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-DLR-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-LDR-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-RDL-Ama-Ama-C/Hcy/Alog, C/Hcy/Alog-Ama-RLD-Ama-Ama-C/Hcy/Alog;

and the compounds:

C/Hcy/Alog-Peptseq-IRE-C/Hcy/Alog, C/Hcy/Alog-Peptseq-IRD-C/Hcy/Alog, C/Hcy/Alog-Peptseq-LRE-C/Hcy/Alog, C/Hcy/Alog-Peptseq-LRD-C/Hcy/Alog, C/Hcy/Alog-Peptseq-ERI-C/Hcy/Alog, C/Hcy/Alog-Peptseq-DRI-C/Hcy/Alog, C/Hcy/Alog-Peptseq-ERL-C/Hcy/Alog, C/Hcy/Alog-Peptseq-DRL-C/Hcy/Alog, C/Hcy/Alog-Peptseq-RIE-C/Hcy/Alog, C/Hcy/Alog-Peptseq-REI-C/Hcy/Alog, C/Hcy/Alog-Peptseq-IER-C/Hcy/Alog, C/Hcy/Alog-Peptseq-EIR-C/Hcy/Alog, C/Hcy/Alog-Peptseq-RLE-C/Hcy/Alog, C/Hcy/Alog-Peptseq-REL-C/Hcy/Alog, C/Hcy/Alog-Peptseq-LER-C/Hcy/Alog, C/Hcy/Alog-Peptseq-ELR-C/Hcy/Alog, C/Hcy/Alog-Peptseq-DIR-C/Hcy/Alog, C/Hcy/Alog-Peptseq-IDR-C/Hcy/Alog, C/Hcy/Alog-Peptseq-RDI-C/Hcy/Alog, C/Hcy/Alog-Peptseq-RID-C/Hcy/Alog, C/Hcy/Alog-Peptseq-DLR-C/Hcy/Alog, C/Hcy/Alog-Peptseq-LDR-C/Hcy/Alog, C/Hcy/Alog-Peptseq-RDL-C/Hcy/Alog, C/Hcy/Alog-Peptseq-RLD-C/Hcy/Alog;

and the compounds:

C/Hcy/Alog-Peptseq-IRE-Peptseq-C/Hcy/Alog, C/Hcy/Alog-Peptseq-IRD-Peptseq-C/Hcy/Alog, C/Hcy/Alog-Peptseq-LRE-Peptseq-C/Hcy/Alog, C/Hcy/Alog-Peptseq-LRD-Peptseq-C/Hcy/Alog, C/Hcy/Alog-Peptseq-ERI-Peptseq-C/Hcy/Alog, C/Hcy/Alog-Peptseq-DRI-Peptseq-C/Hcy/Alog, C/Hcy/Alog-Peptseq-ERL-Peptseq-C/Hcy/Alog, C/Hcy/Alog-Peptseq-DRL-Peptseq-C/Hcy/Alog, C/Hcy/Alog-Peptseq-RIE-Peptseq-C/Hcy/Alog, C/Hcy/Alog-Peptseq-REI-Peptseq-C/Hcy/Alog, C/Hcy/Alog-Peptseq-IER-Peptseq-C/Hcy/Alog, C/Hcy/Alog-Peptseq-EIR-Peptseq-C/Hcy/Alog, C/Hcy/Alog-Peptseq-RLE-Peptseq-C/Hcy/Alog, C/Hcy/Alog-Peptseq-REL-Peptseq-C/Hcy/Alog, C/Hcy/Alog-Peptseq-LER-Peptseq-C/Hcy/Alog, C/Hcy/Alog-Peptseq-ELR-Peptseq-C/Hcy/Alog, C/Hcy/Alog-Peptseq-DIR-Peptseq-C/Hcy/Alog, C/Hcy/Alog-Peptseq-IDR-Peptseq-C/Hcy/Alog, C/Hcy/Alog-Peptseq-RDI-Peptseq-C/Hcy/Alog, C/Hcy/Alog-Peptseq-RID-Peptseq-C/Hcy/Alog, C/Hcy/Alog-Peptseq-DLR-Peptseq-C/Hcy/Alog, C/Hcy/Alog-Peptseq-LDR-Peptseq-C/Hcy/Alog, C/Hcy/Alog-Peptseq-RDL-Peptseq-C/Hcy/Alog, C/Hcy/Alog-Peptseq-RLD-Peptseq-C/Hcy/Alog;

and the compounds:

C/Hcy/Alog-IRE-Peptseq-C/Hcy/Alog, C/Hcy/Alog-IRD-Peptseq-C/Hcy/Alog,

C/Hcy/Alog-LRE-Peptseq-C/Hcy/Alog, C/Hcy/Alog-LRD-Peptseq-C/Hcy/Alog, C/Hcy/Alog-ERI-Peptseq-C/Hcy/Alog, C/Hcy/Alog-DRI-Peptseq-C/Hcy/Alog, C/Hcy/Alog-ERL-Peptseq-C/Hcy/Alog, C/Hcy/Alog-DRL-Peptseq-C/Hcy/Alog, C/Hcy/Alog-RIE-Peptseq-C/Hcy/Alog, C/Hcy/Alog-REI-Peptseq-C/Hcy/Alog, C/Hcy/Alog-IER-Peptseq-C/Hcy/Alog, C/Hcy/Alog-EIR-Peptseq-C/Hcy/Alog, C/Hcy/Alog-RLE-Peptseq-C/Hcy/Alog, C/Hcy/Alog-REL-Peptseq-C/Hcy/Alog, C/Hcy/Alog-LER-Peptseq-C/Hcy/Alog, C/Hcy/Alog-ELR-Peptseq-C/Hcy/Alog, C/Hcy/Alog-DIR-Peptseq-C/Hcy/Alog, C/Hcy/Alog-IDR-Peptseq-C/Hcy/Alog, C/Hcy/Alog-RDI-Peptseq-C/Hcy/Alog, C/Hcy/Alog-RID-Peptseq-C/Hcy/Alog, C/Hcy/Alog-DLR-Peptseq-C/Hcy/Alog, C/Hcy/Alog-LDR-Peptseq-C/Hcy/Alog, C/Hcy/Alog-RDL-Peptseq-C/Hcy/Alog, C/Hcy/Alog-RLD-Peptseq-C/Hcy/Alog;

and the compounds:

Pe-CIREC-Pep, Pe-CIRDC-Pep, Pe-CLREC-Pep, Pe-CLRDC-Pep, Pe-CERIC-Pep, Pe-CDRIC-Pep, Pe-CERLC-Pep, Pe-CDRLC-Pep, Pe-CRIEC-Pep, Pe-CREIC-Pep, Pe-CIERC-Pep, Pe-CEIRC-Pep, Pe-CRLEC-Pep, Pe-CRELC-Pep, Pe-CLERC-Pep, Pe-CELRC-Pep, Pe-CDIRC-Pep, Pe-CIDRC-Pep, Pe-CRDIC-Pep, Pe-CRIDC-Pep, Pe-CDLRC-Pep, Pe-CLDRC-Pep, Pe-CRDLC-Pep, Pe-CRLDC-Pep;

and the compounds:

Pe-C/Hcy/Alog-IRE-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-IRD-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-LRE-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-LRD-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-ERI-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-DRI-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-ERL-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-DRL-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-RIE-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-REI-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-IER-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-EIR-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-RLE-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-REL-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-LER-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-ELR-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-DIR-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-IDR-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-RDI-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-RID-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-DLR-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-LDR-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-RDL-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-RLD-C/Hcy/Alog-Pep;

and the compounds:

Pe-C/Hcy/Alog-Ama-IRE-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-IRD-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-LRE-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-LRD-C/Hcy/Alog-Pep,

Pe-C/Hcy/Alog-Ama-ERI-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-DRI-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-ERL-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-DRL-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-RIE-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-REI-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-IER-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-EIR-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-RLE-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-REL-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-LER-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-ELR-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-DIR-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-IDR-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-RDI-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-RID-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-DLR-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-LDR-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-RDL-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-RLD-C/Hcy/Alog-Pep;

and the compounds:

Pe-C/Hcy/Alog-Ama-Ama-IRE-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-IRD-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-LRE-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-LRD-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-ERI-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-DRI-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-ERL-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-DRL-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-RIE-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-REI-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-IER-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-EIR-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-RLE-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-REL-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-LER-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-ELR-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-DIR-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-IDR-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-RDI-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-RID-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-DLR-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-LDR-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-RDL-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-RLD-C/Hcy/Alog-Pep;

and the compounds:

Pe-C/Hcy/Alog-Ama-Ama-IRE-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-IRD-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-LRE-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-LRD-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-ERI-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-DRI-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-ERL-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-DRL-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-RIE-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-REI-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-IER-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-EIR-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-

Ama-Ama-RLE-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-REL-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-LER-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-ELR-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-DIR-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-IDR-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-RDI-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-RID-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-DLR-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-LDR-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-RDL-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-RLD-Ama-C/Hcy/Alog-Pep;

and the compounds:

Pe-C/Hcy/Alog-Ama-Ama-IRE-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-IRD-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-LRE-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-LRD-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-ERI-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-DRI-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-ERL-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-DRL-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-RIE-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-REI-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-IER-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-EIR-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-RLE-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-REL-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-LER-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-ELR-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-DIR-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-IDR-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-RDI-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-RID-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-DLR-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-LDR-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-RDL-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-Ama-RLD-Ama-Ama-C/Hcy/Alog-Pep;

and the compounds:

Pe-C/Hcy/Alog-IRE-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-IRD-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-LRE-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-LRD-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-ERI-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-DRI-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-ERL-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-DRL-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-RIE-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-REI-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-IER-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-EIR-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-RLE-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-REL-Ama-C/Hcy/Alog-Pep,

Pe-C/Hcy/Alog-LER-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-ELR-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-DIR-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-IDR-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-RDI-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-RID-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-DLR-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-LDR-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-RDL-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-RLD-Ama-C/Hcy/Alog-Pep;

and the compounds:

Pe-C/Hcy/Alog-IRE-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-IRD-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-LRE-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-LRD-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-ERI-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-DRI-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-ERL-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-DRL-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-RIE-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-REI-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-IER-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-EIR-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-RLE-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-REL-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-LER-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-ELR-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-DIR-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-IDR-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-RDI-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-RID-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-DLR-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-LDR-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-RDL-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-RLD-Ama-Ama-C/Hcy/Alog-Pep;

and the compounds:

Pe-C/Hcy/Alog-Ama-IRE-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-IRD-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-LRE-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-LRD-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-ERI-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-DRI-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-ERL-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-DRL-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-RIE-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-REI-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-IER-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-EIR-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-RLE-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-REL-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-LER-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-ELR-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-DIR-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-IDR-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-RDI-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-RID-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-DLR-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-LDR-Ama-

C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-RDL-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-RLD-Ama-C/Hcy/Alog-Pep;

and the compounds:

Pe-C/Hcy/Alog-Ama-IRE-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-IRD-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-LRE-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-LRD-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-ERI-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-DRI-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-ERL-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-DRL-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-RIE-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-REI-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-IER-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-EIR-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-RLE-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-REL-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-LER-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-ELR-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-DIR-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-IDR-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-RDI-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-RID-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-DLR-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-LDR-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-RDL-Ama-Ama-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Ama-RLD-Ama-Ama-C/Hcy/Alog-Pep;

and the compounds:

Pe-C/Hcy/Alog-Peptseq-IRE-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-IRD-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-LRE-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-LRD-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-ERI-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-DRI-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-ERL-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-DRL-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-RIE-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-REI-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-IER-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-EIR-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-RLE-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-REL-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-LER-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-ELR-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-DIR-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-IDR-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-RDI-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-RID-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-DLR-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-LDR-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-RDL-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-RLD-C/Hcy/Alog-Pep;

and the compounds:

Pe-C/Hcy/Alog-Peptseq-IRE-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-IRD-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-LRE-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-LRD-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-ERI-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-DRI-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-ERL-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-DRL-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-RIE-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-REI-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-IER-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-EIR-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-RLE-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-REL-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-LER-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-ELR-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-DIR-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-IDR-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-RDI-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-RID-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-DLR-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-LDR-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-RDL-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-Peptseq-RLD-Peptseq-C/Hcy/Alog-Pep;

and the compounds:

Pe-C/Hcy/Alog-IRE-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-IRD-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-LRE-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-LRD-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-ERI-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-DRI-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-ERL-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-DRL-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-RIE-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-REI-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-IER-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-EIR-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-RLE-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-REL-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-LER-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-ELR-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-DIR-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-IDR-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-RDI-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-RID-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-DLR-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-LDR-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-RDL-Peptseq-C/Hcy/Alog-Pep, Pe-C/Hcy/Alog-RLD-Peptseq-C/Hcy/Alog-Pep;

and the compounds:

Ef-CIREC-Eff, Ef-CIRDC-Eff, Ef-CLREC-Eff, Ef-CLRDC-Eff, Ef-CERIC-Eff, Ef-

CDRIC-Eff, Ef-CERLC-Eff, Ef-CDRLC-Eff, Ef-CRIEC-Eff, Ef-CREIC-Eff, Ef-CIERC-Eff, Ef-CEIRC-Eff, Ef-CRLEC-Eff, Ef-CRELC-Eff, Ef-CLERC-Eff, Ef-CELRC-Eff, Ef-CDIRC-Eff, Ef-CIDRC-Eff, Ef-CRDIC-Eff, Ef-CRIDC-Eff, Ef-CDLRC-Eff, Ef-CLDRC-Eff, Ef-CRDLC-Eff, Ef-CRLDC-Eff;

and the compounds:

Ef-C/Hcy/Alog-IRE-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-IRD-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-LRE-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-LRD-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-ERI-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-DRI-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-ERL-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-DRL-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-RIE-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-REI-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-IER-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-EIR-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-RLE-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-REL-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-LER-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-ELR-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-DIR-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-IDR-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-RDI-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-RID-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-DLR-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-LDR-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-RDL-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-RLD-C/Hcy/Alog-Eff;

and the compounds:

Ef-C/Hcy/Alog-Ama-IRE-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-IRD-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-LRE-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-LRD-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-ERI-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-DRI-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-ERL-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-DRL-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-RIE-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-REI-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-IER-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-EIR-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-RLE-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-REL-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-LER-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-ELR-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-DIR-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-IDR-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-RDI-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-RID-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-DLR-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-LDR-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-RDL-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-RLD-C/Hcy/Alog-Eff;

and the compounds:

Ef-C/Hcy/Alog-Ama-Ama-IRE-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-IRD-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-LRE-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-LRD-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-ERI-C/Hcy/Alog-Eff, Ef-

C/Hcy/Alog-Ama-Ama-DRI-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-ERL-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-DRL-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-RIE-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-REI-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-IER-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-EIR-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-RLE-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-REL-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-LER-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-ELR-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-DIR-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-IDR-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-RDI-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-RID-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-DLR-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-LDR-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-RDL-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-RLD-C/Hcy/Alog-Eff;

and the compounds:

Ef-C/Hcy/Alog-Ama-Ama-IRE-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-IRD-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-LRE-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-LRD-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-ERI-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-DRI-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-ERL-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-DRL-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-RIE-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-REI-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-IER-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-EIR-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-RLE-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-REL-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-LER-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-ELR-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-DIR-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-IDR-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-RDI-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-RID-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-DLR-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-LDR-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-RDL-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-RLD-Ama-C/Hcy/Alog-Eff;

and the compounds:

Ef-C/Hcy/Alog-Ama-Ama-IRE-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-IRD-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-LRE-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-LRD-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-ERI-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-DRI-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-ERL-Ama-Ama-C/Hcy/Alog-Eff, Ef-

C/Hcy/Alog-Ama-Ama-DRL-Ama-Ama-C/Hcy/Alog-Eff; Ef-C/Hcy/Alog-Ama-Ama-RIE-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-REI-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-IER-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-EIR-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-RLE-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-REL-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-LER-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-ELR-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-DIR-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-IDR-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-RDI-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-RID-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-DLR-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-LDR-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-RDL-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-Ama-RLD-Ama-Ama-C/Hcy/Alog-Eff;

and the compounds:

Ef-C/Hcy/Alog-IRE-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-IRD-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-LRE-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-LRD-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-ERI-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-DRI-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-ERL-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-DRL-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-RIE-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-REI-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-IER-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-EIR-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-RLE-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-REL-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-LER-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-ELR-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-DIR-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-IDR-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-RDI-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-RID-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-DLR-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-LDR-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-RDL-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-RLD-Ama-C/Hcy/Alog-Eff;

and the compounds:

Ef-C/Hcy/Alog-IRE-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-IRD-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-LRE-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-LRD-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-ERI-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-DRI-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-ERL-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-DRL-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-RIE-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-REI-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-IER-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-EIR-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-RLE-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-REL-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-LER-Ama-Ama-C/Hcy/Alog-Eff, Ef-

C/Hcy/Alog-ELR-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-DIR-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-IDR-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-RDI-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-RID-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-DLR-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-LDR-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-RDL-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-RLD-Ama-Ama-C/Hcy/Alog-Eff;

and the compounds:

Ef-C/Hcy/Alog-Ama-IRE-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-IRD-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-LRE-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-LRD-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-ERI-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-DRI-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-ERL-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-DRL-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-RIE-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-REI-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-IER-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-EIR-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-RLE-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-REL-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-LER-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-ELR-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-DIR-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-IDR-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-RDI-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-RID-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-DLR-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-LDR-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-RDL-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-RLD-Ama-C/Hcy/Alog-Eff;

and the compounds:

Ef-C/Hcy/Alog-Ama-IRE-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-IRD-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-LRE-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-LRD-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-ERI-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-DRI-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-ERL-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-DRL-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-RIE-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-REI-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-IER-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-EIR-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-RLE-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-REL-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-LER-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-ELR-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-DIR-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-IDR-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-RDI-Ama-Ama-C/Hcy/Alog-

Eff, Ef-C/Hcy/Alog-Ama-RID-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-DLR-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-LDR-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-RDL-Ama-Ama-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Ama-RLD-Ama-Ama-C/Hcy/Alog-Eff;

and the compounds:

Ef-C/Hcy/Alog-Peptseq-IRE-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-IRD-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-LRE-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-LRD-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-ERI-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-DRI-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-ERL-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-DRL-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-RIE-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-REI-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-IER-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-EIR-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-RLE-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-REL-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-LER-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-ELR-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-DIR-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-IDR-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-RDI-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-RID-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-DLR-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-LDR-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-RDL-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-RLD-C/Hcy/Alog-Eff;

and the compounds:

Ef-C/Hcy/Alog-Peptseq-IRE-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-IRD-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-LRE-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-LRD-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-ERI-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-DRI-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-ERL-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-DRL-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-RIE-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-REI-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-IER-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-EIR-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-RLE-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-REL-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-LER-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-ELR-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-DIR-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-IDR-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-RDI-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-RID-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-DLR-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-LDR-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-Peptseq-RDL-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-

Peptseq-RLD-Peptseq-C/Hcy/Alog-Eff;

and the compounds:

Ef-C/Hcy/Alog-IRE-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-IRD-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-LRE-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-LRD-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-ERI-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-DRI-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-ERL-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-DRL-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-RIE-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-REI-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-IER-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-EIR-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-RLE-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-REL-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-LER-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-ELR-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-DIR-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-IDR-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-RDI-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-RID-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-DLR-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-LDR-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-RDL-Peptseq-C/Hcy/Alog-Eff, Ef-C/Hcy/Alog-RLD-Peptseq-C/Hcy/Alog-Eff;

wherein:

each Ama, independently, means a natural amino acid residue or an unnatural amino acid residue comprising maximally 30 non-hydrogen atoms and an unlimited number of hydrogen atoms; and

Pe and Pep, independently of each other and independently of any other structural unit(s)/part(s), are selected from the group of:

natural amino acids/amino acid residues, and

unnatural amino acids/amino acid residues that comprise maximally 35 non-hydrogen atoms and an unlimited number of hydrogen atoms each, and

peptide sequences/residues comprising 2 to 25, preferably 2 to 10, more preferably 2 to 6, and most preferably 2 to 4, natural amino acids/amino acid residues and/or unnatural amino acids/amino acid residues that each comprise maximally 35 non-hydrogen atoms and an unlimited number of hydrogen atoms;

and/or: Pe means that the C/Hcy/Alog to which Pe is connected by a line (-) in the formula

in question is unsubstituted (absence of substituent(s); hydrogen) or Pep means that the C/Hcy/Alog to which Pep is connected by a line (-) in the formula in question is unsubstituted (absence of substituent(s); hydrogen); and

each Peptseq, independently, means: a natural amino acid residue; or an unnatural amino acid residue comprising maximally 30 non-hydrogen atoms and an unlimited number of hydrogen atoms; or a sequence of 2 to 25, preferably 2 to 12, more preferably 2 to 6, still more preferably 2 to 4, and most preferably 3, amino acid residues (peptide units), wherein the amino acid residues are natural amino acid residue(s) and/or unnatural amino acid residue(s) comprising maximally 30 non-hydrogen atoms and an unlimited number of hydrogen atoms;

and wherein in each compound comprising Peptseq at least one, and preferably only one, Peptseq comprises 3 to 25, prefereably 3 to 12, more preferably 3 to 6, still more preferably 3 to 4, and most preferably 3, amino acid residues (peptide units); and

and wherein each C/Hcy/Alog, independently, means: cysteine; or homocysteine; or a homologue or branched homologue thereof comprising no more than 15, preferably no more than 12, more preferably no more than 10, carbon atoms; and

wherein Ef and Eff, independently, are selected from the group of:

effector units, linker units, solubility modifier units, stabilizer units, charge modifier units, spacer units, lysis and/or reaction and/or reactivity modifier units, internalizing and/or internalization enhancer and/or membrane interaction units and/or other local route and/or local attachment/local binding and/or distribution affecting units, adsorption enhancer units, and other related units, and

amino acids and peptides and other structures that comprise one or more such said unit(s);

and/or: Ef means that the C/Hcy/Alog to which Ef is connected by a line (-) in the formula in question is unsubstituted (absence of substituent(s); hydrogen) or Eff means that the C/Hcy/Alog to which Eff is connected by a line (-) in the formula in question is unsubstituted (absence of substituent(s); hydrogen); and

and wherein any amino acid(s) may comprise L amino acid(s) and/or D amino acid(s) and/or any other optical isomer(s);

in any of which optionally:

a disulphide bridge exists between thiol groups, and/or
a disulphide bridge does not exist between thiol groups, and/or
the presence/number of disulphide bridge(s) is undetermined and/or uncertain and/or fluctuating and/or variable and/or subject to change and/or fluctuation and/or uncomplete and/or partial;

and:

- any salt(s)
- any ester(s)
- any amide(s)
- any hydrazide(s)
- any *N*-substituted amide(s)
- any *N*-substituted hydrazide(s)
- any hydroxamic acid derivative(s)
- any decarboxylated analogue(s)
- any *N*-substituted derivative(s)
- any other related derivative(s)
- any other related analogue(s)
- any protected derivative(s) and analogue(s)
- any activated derivative(s) and analogue(s)
- any resin-bound derivative(s) and analogue(s)
- any combination(s) of any of such salt, derivative and/or analogue types

of any of said compounds.

144. Compounds according to claim 142 or claim 143, wherein the effector unit(s) and/or one or more thereof is/are selected from the effector units according to and/or mentioned in any one(s) of claims 34-38 and/or in claim 44 and/or claim 45.

145. Compounds characterized in that they:

comprise one or/more of the compounds according to any one of claims 123 to 144, as structural part(s)/unit(s)/radical(s)/group(s)/their like, wherein said compound(s) according to any one of claims 123 to 144 may and/or may not be connected/bound/bonded through any type(s) of bond(s) and/or may linkage(s), preferably by one or more peptide and/or amide bond(s); and

also comprise one or more atom(s) that are selected from the group of all atoms and isotopes and elements; and

have a molecular/formula weight not exceeding 15000, preferably not exceeding 5000, more preferably not exceeding 3000, still more preferably not exceeding 2300; and

preferably comprise one or more effector group(s), more preferably effector group(s) having one or more therapeutic and/or diagnostic property/properties and/or application(s) and/or biological activity/activities;

and:

- any salt(s)
- any ester(s)
- any amide(s)
- any hydrazide(s)
- any *N*-substituted amide(s)
- any *N*-substituted hydrazide(s)
- any hydroxamic acid derivative(s)
- any decarboxylated analogue(s)
- any *N*-substituted derivative(s)
- any other related derivative(s)
- any other related analogue(s)
- any protected derivative(s) and analogue(s)
- any activated derivative(s) and analogue(s)
- any resin-bound derivative(s) and analogue(s)
- any combination(s) of any of such salt, derivative and/or analogue types

of any of said compounds.

146. Compounds characterized in that they:

comprise one or/more of the compounds according to any one of claims 123 to 145, as structural part(s)/unit(s)/radical(s)/group(s)/their like, wherein said compound(s) according to any one of claims 123 to 145 may and/or may not be connected/bound/bonded through any type(s) of bond(s) and/or may linkage(s), preferably by one or more peptide and/or amide bond(s); and

also comprise one or more atom(s) that are selected from the group of all atoms and isotopes and elements; and

also comprise one or more biological and/or other macromolecule(s) and/or part(s) and/or fragment(s) and/or radical(s) and/or analogue(s) and/or derivative(s) thereof, preferably protein(s) and/or one or more type(s) of nucleic acid(s) and/or nucleic acid analogue(s) and/or derivative(s); and

preferably have a molecular/formula weight not exceeding 1.000.000, more preferably not exceeding 500.000, still more preferably not exceeding 300.000, still more preferably not exceeding 120.000; and

preferably comprise one or more effector group(s), more preferably effector group(s) having one or more therapeutic and/or diagnostic property/properties and/or application(s) and/or biological activity/activities;

and:

- any salt(s)
- any ester(s)
- any amide(s)
- any hydrazide(s)
- any *N*-substituted amide(s)
- any *N*-substituted hydrazide(s)
- any hydroxamic acid derivative(s)
- any decarboxylated analogue(s)
- any *N*-substituted derivative(s)
- any other related derivative(s)
- any other related analogue(s)
- any protected derivative(s) and analogue(s)
- any activated derivative(s) and analogue(s)
- any resin-bound derivative(s) and analogue(s)
- any combination(s) of any of such salt, derivative and/or analogue types

of any of said compounds.

147. Activated and/or protected and/or resin-bound and/or related forms, derivatives and analogues of the compound(s) according to any one of claims 123 to 146,

and:

- any salt(s)
- any ester(s)

- any amide(s)
- any hydrazide(s)
- any *N*-substituted amide(s)
- any *N*-substituted hydrazide(s)
- any hydroxamic acid derivative(s)
- any decarboxylated analogue(s)
- any *N*-substituted derivative(s)
- any other related derivative(s)
- any other related analogue(s)
- any protected derivative(s) and analogue(s)
- any activated derivative(s) and analogue(s).
- any resin-bound derivative(s) and analogue(s)
- any combination(s) of any of such salt, derivative and/or analogue types

of any of them.

148. A diagnostic composition comprising at least one targeting agent according to any one of claims 1-49 and/or at least one targeting unit according to any one of claims 50-87 and/or at least one targeting motif according to 88-112 and/or at least one peptide and/or peptidomimetic analogue and/or peptidyl analogue according to any one of claims 113-121 and/or at least one compound according to 123-146, and/or at least one salt and/or derivative and/or analogue of one or more of them according to any one of the previous claims, and optionally also one or more diagnostically and/or pharmaceutically acceptable carrier(s) and/or labelling agent(s) and/or solvent(s) and/or vehichle(s) and/or additive(s) and/or their like.

149. A pharmaceutical composition comprising at least one targeting agent according to any one of claims 1-49 and/or at least one targeting unit according to any one of claims 50-87 and/or at least one targeting motif according to 88-112 and/or at least one peptide and/or peptidomimetic analogue and/or peptidyl analogue according to any one of claims 113-121 and/or at least one compound according to 123-146, and/or at least one salt and/or derivative and/or analogue of one or more of them according to any one of the previous claims, and optionally also one or more pharmaceutically acceptable carrier(s) and/or labelling agent(s) and/or solvent(s) and/or vehichle(s) and/or additive(s) and/or their like.

150. A diagnostic and pharmaceutical composition, intended for therapeutic use and for diagnostic use and/or for both of them, comprising at least one targeting agent according to any one of claims 1-49 and/or at least one targeting unit according to any one of claims 50-87 and/or at least one targeting motif according to 88-112 and/or at least one peptide and/or

peptidomimetic analogue and/or peptidyl analogue according to any one of claims 113-121and/or at least one compound according to 123-146, and/or at least one salt and/or derivative and/or analogue of one or more of them according to any one of the previous claims, and optionally also one or more diagnostically and/or pharmaceutically acceptable carrier(s) and/or labelling agent(s) and/or solvent(s) and/or vehichle(s) and/or additive(s) and/or their like.

151. A pharmaceutical composition according to claim 107 and/or a diagnostic composition according to claim 106 and/or a diagnostic and pharmaceutical composition according to claim 108, wherein one or more nucleus/nuclei/radioisotope(s) is/are used that is/are capable of emitting radiation.

152. A pharmaceutical composition according to claim 150, 151 or 152, and/or a diagnostic composition according to claim 148, 151 or 152, and/or a diagnostic and pharmaceutical composition according to claim 150 to 152, wherein one or more nucleus/nuclei/radioisotope(s) is/are used that is/are capable of emitting alpha and/or beta and/or gamma and/or positron and/or related particle(s)/photon(s)/radiation(s); in the case of the pharmaceutical composition preferably alpha particle(s)/radiation(s).

153. A kit for treating and/or diagnosing and/or confirming and/or excluding and/or studying and/or evaluating and/or studying and/or imaging, and/or making the differential diagnosis of, cancer and/or its metastasis/metastases and/or tumor cells and/or tumor endothelium and/or angiogenic/neoangiogenic endothelium and/or disease(s) and/or organ(s) and/or tissue(s), optionally *in vivo* and/or *in vitro* and/or *ex vivo* and/or *in situ*, comprising at least one targeting agent according to any one of claims 1-49 and/or at least one targeting unit according to any one of claims 50-87 and/or at least one targeting motif according to any one of claims 88-112 and/or at least one peptide and/or peptidomimetic analogue and/or peptidyl analogue according to any one of claims 113-121 and/or at least one compound according to 123-146, and/or at least one salt and/or derivative and/or analogue of one or more of them according to any one of the previous claims, and/or at least one pharmaceutical composition according to any one of claims 149, 151 or 152 and/or at least one diagnostic composition according to to any one of claims 148, 151 or 152 and/or at least one diagnostic and pharmaceutical composition according to to any one of claims 150 to 152 and/or at least one material and/or substance comprising one or more of the aforementioned; and optionally one or more other material(s) and/or substance(s).

154. A kit for cell sorting and/or cell removal and/or cell enrichment and/or cell selection and/or cell collection, and/or quantitation of cells, and/or for qualitative classification of cells and/or for related purpose(s), characterized in that it comprises one or more targeting

motif(s) according to 88-112 and/or one or more targeting unit(s) according to 50-87 and/or one or more targeting agent(s) according to 1-49 and/or one or more peptide(s) and/or peptidomimetic analogue(s) and/or peptidyl analogue(s) according to any one of claims 113-121 and/or at least one compound according to 123-146, and/or at least one salt and/or derivative and/or analogue of one or more of them according to any one of the previous claims, and/or one or more pharmaceutical composition(s) according to claims 149, 151 or 152 and/or one or more diagnostic composition(s) according to any one of claims 148, 151 or 152 and/or one or more diagnostic and pharmaceutical composition(s) according to any one of claims 150 to 152 and/or one or more material(s) comprising one or more of the aforementioned; and optionally one or more other material(s) and/or substance(s).

155. A kit for research purposes and/or investigation(s) and/or scientific use(s) and/or science purpose(s) and/or basic research purpose(s) and/or use(s), and/or their like, characterized in that it comprises one or more targeting motif(s) according to 88 to 112 and/or one or more targeting unit(s) according to 50-87 and/or one or more targeting agent(s) according to 1-49 and/or one or more peptide(s) and/or peptidomimetic analogue(s) and/or peptidyl analogue(s) according to any one of claims 113-121 and/or at least one compound according to 123-146, and/or at least one salt and/or derivative and/or analogue of one or more of them according to any one of the previous claims, and/or one or more pharmaceutical composition(s) according to claims 149, 151 or 152 and/or one or more diagnostic composition(s) according to any one of claims 148, 151 or 152 and/or one or more diagnostic and pharmaceutical composition(s) according to any one of claims 150 to 152 and/or one or more material(s) comprising one or more of the aforementioned; and optionally one or more other material(s) and/or substance(s).

156. A method for treating and/or diagnosing cancer and/or cancer metastasis/metastases and/or tumor(s) and/or malignant disease(s) and/or malignancy/malignancies and/or leukemia(s) and/or other proliferative blood/haematological disease(s) and/or processes and/or their like and/or other lymphoproliferative and/or other proliferative diseases and/or state(s) and/or disorder(s) and/or their like and/or angiogenesis and/or neoangiogenesis and/or tumor/cancer endothelium and/or angiogenic/neoangiogenic endothelium and/or disease(s) and/or process(es) and/or organ(s) and/or tissue(s) and/or malignant and/or transformed and/or cancer and/or tumor and/or leukeamia/leukemic and/or related cells and/or tissue(s) and/or organ(s), and/or for excluding and/or evaluating and/or studying and/or investigating and/or excluding one or more of them, and/or making differential diagnosis of one or more of them; comprising administering to a human or animal at least one targeting agent according to any one of claims 1 to 49 and/or at least one targeting unit according to any one of claims 50 to 87 and/or at least one targeting motif according to any

one of claims 88 to 112 and/or at least one peptide and/or peptidomimetic analogue and/or peptidyl analogue according to any one of claims 113 to 121 and/or at least one compound according to any one of claims 123 to 146, and/or at least one salt and/or derivative and/or analogue of one or more of them according to any one of the previous claims, and/or at least one pharmaceutical composition according to 149, 151 or 152 and/or at least one diagnostic composition according to any one of claims 148, 151 or 152 and/or at least one diagnostic and pharmaceutical composition according to any one of claims 150 to 152, in an effective amount.

157. A method for treating and/or diagnosing cancer or cancer metastasis/metastases and/or angiogenic/neoangiogenic endothelium and/or disease(s) and/or organ(s) and/or tissue(s), and/or excluding and/or evaluating and/or studying and/or investigating one or more of them, and/or making differential diagnosis of one or more of them, comprising administering to a biological sample/material/organ/tissue/blood/part and/or their like that is/are from a human or from an animal, at least one targeting agent according to any one of claims 1 to 49 and/or at least one targeting unit according to any one of claims 50 to 87 and/or at least one targeting motif according to any one of claims 88 to 112 and/or at least one peptide and/or peptidomimetic analogue and/or peptidyl analogue according to any one of claims 113 to 121 and/or at least one compound according to any one of claims 123 to 146 and/or at least one pharmaceutical composition according to any one of claims 149, 151 or 152 and/or at least one diagnostic composition according to to any one of claims 148, 151 or 152 and/or at least one diagnostic and pharmaceutical composition according to to any one of claims150 to 152 and/or one or more or all component(s)/content(s) of one or more kit(s) according to any one of claims to any one of claims, and optionally also involving other treatment(s) and/or manipulation(s) and/or procedure(s) and/or administration(s) and/or material(s) and/or chemical(s) and/or their like.

158. A method according to claim 156 or 157, wherein cell sorting and/or removal and/or enrichment and/or selection and/or their like, and/or targeted destruction and/or therapy and/or treatment and/or killing and/or inactivation and/or their like, is involved and/or employed and/or made use of and/or applied and/or effected.

159. The therapeutic use of any of the product(s)/material(s) according to any one of claims 1 to 155.

160. The diagnostic use of any of the product(s)/material(s) according to any one of claims 1 to 155.

161. The therapeutic use of any of the product(s)/material(s) according to any one of claims

1 to 155, *in vivo* and/or *in vitro* and/or *ex vivo* and/or *in situ* and/or *ex situ*.

162. The diagnostic use of any of the product(s)/material(s) according to any one of claims 1 to 155, *in vivo* and/or *in vitro* and/or *ex vivo* and/or *in situ* and/or *ex situ*.

163. The use of any of the product(s)/material(s) according to any one of claims 1 to 155 for diagnosis and/or for therapy and/or for diagnostic and/or therapeutic purpose(s) and/or application(s) and/or goal(s) and/or procedure(s) and/or method(s) and/or technique(s) and/or process(es) and/or their like and/or for similar and/or related purpose(s).

164. The use of any of the product(s)/material(s) according to any one of claims 1 to 155 for diagnosis and/or for therapy and/or for diagnostic and/or therapeutic purpose(s) and/or application(s) and/or goal(s) and/or procedure(s) and/or method(s) and/or technique(s) and/or process(es) and/or their like and/or for similar and/or related purpose(s), *in vivo* and/or *in vitro* and/or *ex vivo* and/or *in situ* and/or *ex situ*.

165. The use of the targeting agent according to any one of claims 1 to 49 and/or the targeting unit according to any one of claims 50 to 87 and/or the targeting motif according to any one of claims 88 to 112 and/or the peptide(s), peptidomimetic analogue(s) and/or peptidyl analogue(s) according to any one of claims 113 to 121 and/or the compound(s) according to any one of claims 123 to 146, and/or salt(s) and/or derivative(s) and/or analogue(s) of one or more of them according to any one of claims 122 or 147, and/or any combination(s) thereof, and/or any material(s) and/or combination(s) of materials comprising one or more of the aforementioned, as a medicine/drug/pharmaceutical and/or diagnostic agent/substance/material/drug administered *in vivo* to a human/humans and/or to an animal/animals, and/or *in vitro* and/or *ex vivo* and/or *in situ* and/or *ex situ* and/or otherwise.

166. The use of the targeting agent according to any one of claims 1 to 49 and/or the targeting unit according to any one of claims 50 to 87 and/or targeting motif according to any one of claims 88 to 112 and/or the peptide(s) and/or peptidomimetic analogue(s) and/or peptidyl analogue(s) according to any one of claims 113 to 121 and/or the compound(s) according to any one of claims 123 to 146, and/or salt(s) and/or derivative(s) and/or analogue(s) of one or more of them according to any one of claims 122 or 147, and/or the kit according to any one of claims 153 to 155, and/or any combination(s) thereof, and/or any material(s) comprising at least one of the aforementioned:

for the preparation of a
medicament/medicine/drug/preparation/composition/pharmaceutical for the treatment of

cancer and/or cancer metastasis/metastases and/or tumor(s) and/or malignant disease(s) and/or malignancy/malignancies and/or leukemia(s) and/or other proliferative blood/haematological disease(s) and/or processes and/or their like and/or other lymphoproliferative and/or other proliferative diseases and/or state(s) and/or disorder(s) and/or their like and/or angiogenesis and/or neoangiogenesis and/or tumor/cancer endothelium and/or angiogenic/neoangiogenic endothelium and/or disease(s) and/or process(es) and/or organ(s) and/or tissue(s) and/or malignant and/or transformed and/or cancer and/or tumor and/or leukeamia/leukemic and/or related cells and/or tissue(s) and/or organ(s), *in vivo* and/or *in vitro* and/or *ex vivo* and/or *in situ* and/or *ex situ* and/or otherwise;

for the preparation of a medicament/medicine/drug/preparation/composition/pharmaceutical for the targeted treatment of cancer pain/cancer-related pain and/or related pain(s) *in vivo*; and/or

as a diagnostic agent, *in vivo* and/or *in vitro* and/or *ex vivo* and/or *in situ* and/or *ex situ* and/or otherwise; and/or

as a therapeutic/pharmaceutical agent *in vivo* or *in vitro* and/or *ex vivo* and/or *in situ* and/or *ex situ* and/or otherwise; and/or

for the preparation of a reagent/reagents and/or diagnostic agent(s) to be used for the diagnosis and/or confirmation and/or exclusion and/or evaluation and/or investigation and/or study of cancer and/or cancer metastasis/metastases and/or tumor(s) and/or malignant disease(s) and/or malignancy/malignancies and/or leukemia(s) and/or other proliferative blood/haematological disease(s) and/or processes and/or their like and/or other lymphoproliferative and/or other proliferative diseases and/or state(s) and/or disorder(s) and/or their like and/or angiogenesis and/or neoangiogenesis and/or tumor/cancer endothelium and/or angiogenic/neoangiogenic endothelium and/or disease(s) and/or process(es) and/or organ(s) and/or tissue(s) and/or malignant and/or transformed and/or cancer and/or tumor and/or leukeamia/leukemic and/or related cells and/or tissue(s) and/or organ(s), *in vivo* and/or *in vitro* and/or *ex vivo* and/or *in situ* and/or *ex situ* and/or otherwise.

167. The use of the targeting motif according to any one of claims 88 to 112 and/or the targeting agent according to any one of claims 1 to 49 and/or the targeting unit according to any one of claims 50 to 87 and/or the peptide(s) and/or peptidyl analogue(s) and/or peptidomimetic analogue(s) according to any one of claims 113 to 121 and/or the compound(s) according to any one of claims 123 to 146, and/or salt(s) and/or derivative(s)

and/or analogue(s) of one or more of them according to any one of claims 122 or 147, and/or the kit according to any one of claims 153 to 155, and/or a substance and/or material and/or molecule and/or product and/or polymer and/or their like comprising one or more of the aforementioned, for targeting.

168. The use of the targeting motif according to any one of claims 88 to 112 and/or the targeting agent according to any one of claims 1to 49 and/or the targeting unit according to any one of claims 50 to 87 and/or the peptide(s) and/or peptidyl analogue(s) and/or peptidomimetic analogue(s) according to any one of claims 113 to 121 and/or the kit according to any one of claims 153 to 155, and/or a substance and/or material and/or molecule and/or product and/or polymer and/or their like comprising one or more of the aforementioned, for tumor targeting and/or tumor cell targeting and/or metastasis targeting and/or tumor endothelium targeting and/or angiogenic/neoangiogenic endothelium/ disease/organ/tissue targeting, *in vivo* and/or *in vitro*, and/or for targeting cancer and/or cancer metastasis/metastases and/or tumor(s) and/or malignant disease(s) and/or malignancy/malignancies and/or leukemia(s) and/or other proliferative blood/haematological disease(s) and/or processes and/or their like and/or other lymphoproliferative and/or other proliferative diseases and/or state(s) and/or disorder(s) and/or their like and/or angiogenesis and/or neoangiogenesis and/or tumor/cancer endothelium and/or angiogenic/neoangiogenic endothelium and/or disease(s) and/or process(es) and/or organ(s) and/or tissue(s) and/or malignant and/or transformed and/or cancer and/or tumor and/or leukeamia/leukemic and/or related cells and/or tissue(s) and/or organ(s), *in vivo* and/or *in vitro* and/or *ex vivo* and/or *in situ* and/or *ex situ* and/or otherwise.

169. The use of the targeting motif according to any one of claims 88 to 112 and/or a substance and/or material and/or molecule and/or product and/or polymer and/or their like comprising it,

for tumor targeting *in vivo* and/or *in vitro*, and/or for tumor cell targeting *in vitro*, and/or for tumor and/or tumor endothelium and/or tumor mass and/or metastasis targeting *in vivo* and/or *in vitro*, and/or for angiogenic/neoangiogenic endothelium and/or disease and/or organ and/or tissue targeting *in vivo* and/or *in vitro*, and/or for the preparation and/or synthesis of one or more tumor targeting unit(s) and/or tumor targeting agent(s) and/or other material(s) and/or substance(s) intended for tumor and/or tumor cell and/or tumor endothelium and/or tumor mass and/or metastasis and/or angiogenic/neoangiogenic endothelium/disease/organ/tissue targeting *in vitro* and/or *in vivo*; and/or

for targeting cancer and/or cancer metastasis/metastases and/or tumor(s) and/or malignant

disease(s) and/or malignancy/malignancies and/or leukemia(s) and/or other proliferative blood/haematological disease(s) and/or processes and/or their like and/or other lymphoproliferative and/or other proliferative diseases and/or state(s) and/or disorder(s) and/or their like and/or angiogenesis and/or neoangiogenesis and/or tumor/cancer endothelium and/or angiogenic/neoangiogenic endothelium and/or disease(s) and/or process(es) and/or organ(s) and/or tissue(s) and/or malignant and/or transformed and/or cancer and/or tumor and/or leukeamia/leukemic and/or related cells and/or tissue(s) and/or organ(s), *in vivo* and/or *in vitro* and/or *ex vivo* and/or *in situ* and/or *ex situ* and/or otherwise; and/or for the preparation and/or synthesis of one or more targeting unit(s) and/or targeting agent(s) and/or other material(s) and/or substance(s) intended for targeting cancer and/or cancer metastasis/metastases and/or tumor(s) and/or malignant disease(s) and/or malignancy/malignancies and/or leukemia(s) and/or other proliferative blood/haematological disease(s) and/or processes and/or their like and/or other lymphoproliferative and/or other proliferative diseases and/or state(s) and/or disorder(s) and/or their like and/or angiogenesis and/or neoangiogenesis and/or tumor/cancer endothelium and/or angiogenic/neoangiogenic endothelium and/or disease(s) and/or process(es) and/or organ(s) and/or tissue(s) and/or malignant and/or transformed and/or cancer and/or tumor and/or leukeamia/leukemic and/or related cells and/or tissue(s) and/or organ(s), *in vivo* and/or *in vitro* and/or *ex vivo* and/or *in situ* and/or *ex situ* and/or otherwise; and/or

as part(s) and/or moiety/moieties of and/or as constituent(s) of one or more targeting unit(s) and/or targeting agent(s) and/or tageting polymer(s) and/or resin(s) and/or related materials and/or other material(s) and/or substance(s) and/or kit(s) intended for targeting cancer and/or cancer metastasis/metastases and/or tumor(s) and/or malignant disease(s) and/or malignancy/malignancies and/or leukemia(s) and/or other proliferative blood/haematological disease(s) and/or processes and/or their like and/or other lymphoproliferative and/or other proliferative diseases and/or state(s) and/or disorder(s) and/or their like and/or angiogenesis and/or neoangiogenesis and/or tumor/cancer endothelium and/or angiogenic/neoangiogenic endothelium and/or disease(s) and/or process(es) and/or organ(s) and/or tissue(s) and/or malignant and/or transformed and/or cancer and/or tumor and/or leukeamia/leukemic and/or related cells and/or tissue(s) and/or organ(s), *in vivo* and/or *in vitro* and/or *ex vivo* and/or *in situ* and/or *ex situ* and/or otherwise; and/or

for the preparation and/or synthesis of, and/or as part(s) of and/or as constituent(s) of, one or more tumor targeting medicinal(s) and/or tumor targeting pharmaceutical(s) and/or other diagnostic and/or therapeutic material(s) and/or substance(s) intended for tumor and/or tumor cell and/or tumor endothelium and/or tumor mass and/or metastasis targeting *in vitro*

and/or *in vivo* and/or for tumor and/or metastasis diagnostics and/or therapy, and/or for any their like use(s) and/or for targeting and/or diagnostics and/or therapy of cancer and/or cancer metastasis/metastases and/or tumor(s) and/or malignant disease(s) and/or malignancy/malignancies and/or leukemia(s) and/or other proliferative blood/haematological disease(s) and/or processes and/or their like and/or other lymphoproliferative and/or other proliferative diseases and/or state(s) and/or disorder(s) and/or their like and/or angiogenesis and/or neoangiogenesis and/or tumor/cancer endothelium and/or angiogenic/neoangiogenic endothelium and/or disease(s) and/or process(es) and/or organ(s) and/or tissue(s) and/or malignant and/or transformed and/or cancer and/or tumor and/or leukeamia/leukemic and/or related cells and/or tissue(s) and/or organ(s), *in vivo* and/or *in vitro* and/or *ex vivo* and/or *in situ* and/or *ex situ* and/or otherwise.

170. The use of the targeting motif according to any one claims 88 to 112 and/or the targeting unit according to 50 to 87 and/or the targeting agent according to any one claims 1 to 49 and/or the peptide(s) and/or peptidomimetic analogue(s) and/or peptidyl analogue(s) according to any one claims 113 to 121 and/or the compound(s) according to any one claims 123 to 146, and/or salt(s) and/or derivative(s) and/or analogue(s) of one or more of them according to any one of claims 122 or 147, and/or the kit according to any one of claims 153 to 155, and/or a substance and/or material and/or molecule and/or product and/or polymer and/or their like comprising one or more of the aforementioned:

for cell sorting and/or cell removal and/or cell enrichment and/or cell selection and/or cell collection and/or quantitation of cells and/or for qualitative classification of cells, and/or for related purpose(s); and/or

for the isolation and/or partial and/or total purification and/or identification and/or production of cellular and/or molecular and/or related biological target(s) thereof; and/or

in and/or for histology and/or cytology and/or cytochemistry and/or immunohistology and/or microscopy and/or electron microscopy and/or related field(s), technique(s) and/or methodolgy/methodologies; and/or

in histology and/or cytology and/or cytochemistry and/or immunohistology and/or microscopy and/or electron microscopy and/or related field(s), technique(s) and/or methodolgy/methodologies, for the purpose(s) of research, staining, characterization, diagnosis, investigation, detection and/or any related purpose(s); and/or

as reagent(s) and/or component(s) of reagent(s) and/or reagent mixture(s) and/or kit(s) and/or other material(s) in histology and/or cytology and/or cytochemistry and/or immunohistology and/or microscopy and/or electron microscopy and/or related field(s), technique(s) and/or methodolgy/methodologies, for the purpose(s) of research, staining, characterization, diagnosis, investigation, detection and/or any related purpose(s); and/or

in vitro and/or *in vivo*, as antigen(s) and/or as immunogen(s) and/or for immunization(s) and/or for the preparation of antiserum/antisera and/or antibody/antibodies and/or vaccine(s) and/or related product(s) and/or material(s).

171. The therapeutic and/or related use(s), and/or the diagnostic and/or related use(s), and/or the simultaneous therapeutic/related use(s) and diagnostic/related use(s), of one or more of the targeting agent(s) according to any one of claims 1 to 49 and/or the targeting unit(s) according to any one of claims 50 to 87 and/or the targeting motif(s) according to any one of claims 88 to 112 and/or the peptide(s) and/or peptidyl analogue(s) and/or peptidomimetic analogue(s) according to any one of claims 113 to 121 and/or the pharmaceutical and/or diagnostic and/or the diagnostic and pharmaceutical compositions according to any one of claims 148 to 152 and/or the kit(s) according to any one of claims 153 to 155, and/or of any substance(s), material(s), compound(s), mixture(s), composition(s) and/or other product(s) and/or preparation(s) comprising one or more of them as such and/or as any salt(s) and/or derivative(s) thereof and/or as substructure(s) and/or part(s) of one or more chemical structure(s) and/or molecule(s) and/or ion(s) and/or substance(s) and/or material(s) and/or polyner(s) and/or their like, *in vivo* and/or *in vitro* and/or *ex vivo* and/or *in situ* and/or *ex situ* and/or otherwise, for therapy of cancer and/or cancer metastasis/metastases and/or tumor(s) and/or malignant disease(s) and/or malignancy/malignancies and/or leukemia(s) and/or other proliferative blood/haematological disease(s) and/or processes and/or their like and/or other lymphoproliferative and/or other proliferative diseases and/or state(s) and/or disorder(s) and/or their like and/or angiogenesis and/or neoangiogenesis and/or tumor/cancer endothelium and/or angiogenic/neoangiogenic endothelium and/or disease(s) and/or process(es) and/or organ(s) and/or tissue(s) and/or malignant and/or transformed and/or cancer and/or tumor and/or leukeamia/leukemic and/or related cells and/or tissue(s) and/or organ(s).

172. The therapeutic and/or related use(s), and/or the diagnostic and/or related use(s), and/or the simultaneous therapeutic/related use(s) and diagnostic/related use(s) according to any one of claims 159 to 171,

wherein one or more of the targeting agent(s) according to any one of claims 1 to 49 and/or

the targeting unit(s) according to any one of claims 50 to 87 and/or the targeting motif(s) according to any one of claims 88 to 112 and/or the peptide(s) and/or peptidyl analogue(s) and/or peptidomimetic analogue(s) according to any one of claims113 to 121 and/or the compound(s) according to any one of claims123 to 146, and/or salt(s) and/or derivative(s) and/or analogue(s) of one or more of them according to claim 122 or 147, and/or the pharmaceutical and/or diagnostic and/or the diagnostic and pharmaceutical compositions according to any one of claims 148 to 152 and/or the kit(s) according to any one of claims 153 to 155, and/or of any substance(s), material(s), compound(s), mixture(s), composition(s) and/or other product(s) and/or preparation(s) comprising one or more of them as such and/or as any salt(s) and/or derivative(s) thereof and/or as substructure(s) and/or part(s) of one or more chemical structure(s) and/or molecule(s) and/or ion(s) and/or substance(s) and/or material(s) and/or polyner(s) and/or their like; and/or part(s) of one or more of the aforementioned; comprise(s): one or more radioactive nucleus/nuclei and/or particle(s) and/or cluster(s) and/or their like, and/or one or more paramagnetic atom(s) and/or other moiety/moieties and/or particle and/or their like, and/or boron atom(s) and/or isotope-enriched boron;

and/or

one or more natural and/or artificial nucleus/nuclei capable of emitting alpha radiation is employed/involved/used, *in vivo* and/or *in vitro*;

and/or

that is/are used, employed, intended, intended to be used, aimed and/or involved for diagnosis and/or exclusion and/or confirmation and/or evaluation and/or other investigation(s) and/or study of cancer and/or cancer metastasis/metastases and/or tumor(s) and/or malignant disease(s) and/or malignancy/malignancies and/or leukemia(s) and/or other proliferative blood/haematological disease(s) and/or processes and/or their like and/or other lymphoproliferative and/or other proliferative diseases and/or state(s) and/or disorder(s) and/or their like and/or angiogenesis and/or neoangiogenesis and/or tumor/cancer endothelium and/or angiogenic/neoangiogenic endothelium and/or disease(s) and/or process(es) and/or organ(s) and/or tissue(s) and/or malignant and/or transformed and/or cancer and/or tumor and/or leukeamia/leukemic and/or related cells and/or tissue(s) and/or organ(s), *in vivo* and/or *in vitro* and/or *ex vivo* and/or *in situ* and/or *ex situ* and/or otherwise;

and/or

the use(s) comprise(s) use(s) in/for/involving imaging(s) and/or spectroscopy/spectroscopies and/or magnetic resonance method(s) and/or positron emission tomography and/or other positron emission method(s) and/or SPECT method(s) and/or cytology and/or histology and/or microscopy and/or electron microscopy and/or tunnelling microscopy and/or atomic force microscopy and/or any form of microscopy and/or FACS method(s) and/or fluorescence method(s) and/or phosphorescence method(s) and/or isotope method(s) and/or the use of radioactive isotope(s) and/or cell counting and/or sorting and/or their like and/or gamma radiation method(s) and/or NMRI method(s) and/or other MRI method(s) and/or NMR spectroscopy and/or EPR/ESR spectroscopy *in vivo* and/or *in vitro* and/or *ex vivo* and/or *in situ* and/or *ex situ* and/or otherwise.

173. The use of the structure and/or motif and/or compound and/or substance and/or sequence Dd-Ee-Ff for targeting and/or as a targeting motif and/or targeting unit and/or for the purpose of targeting and/or to effect/cause/give rise to targeting and/or targeted delivery and/or administration and/or transport and/or therapy and/or diagnosis and/or action and/or effect and/or their like;
wherein

Dd is either Aa or Bb or Cc or Aa′ or Bb′ or Cc′, and
Ee is either Aa or Bb or Cc or Aa′ or Bb′ or Cc′, and
Ff is either Aa or Bb or Cc or Aa′ or Bb′ or Cc′, and
Dd-Ee-Ff comprises Aa/Aa′and Bb/Bb′ and Cc/Cc′, and

and/or Dd-Ee-Ff is a structural and/or functional analogue of a structure or structures where Dd-Ee-Ff is as defined above;

wherein

Aa is the L- or D- form of isoleucine, leucine, *tert*-leucine or valine, or a structural and/or functional analogue thereof comprising in its side chain a branched, non-branched and/or alicyclic structure with at least two similar or different atoms selected from the group of carbon atoms, silicon atoms, halogen atoms bonded to one or more carbon(s), ether-oxygens and thioether-sulphurs;

Bb is the L- or D- form of arginine, homoarginine or canavanine, or a structural and/or functional analogue thereof comprising at least one guanyl and/or amidino group or a related group that has or can through protonation obtain a delocalized positive charge;

Cc is the L- or D- form of glutamic acid or aspartic acid, or a structural and/or functional

analogue thereof, comprising in its side chain at least one carboxyl group or esterified carboxyl group;

Aa′ is a branched or non-branched or cyclic non-aromatic, lipophilic and/or hydrophobic amino acid or amino acid analogue or derivative or a structural and/or functional analogue thereof, or an amino acid or carboxylic acid or amino acid analogue or derivative or carboxylic acid analogue or derivative that has one or more lipophilic carborane-type and/or other lipophilic boron-containing side chain(s) or its/their equivalent(s) or another lipophilic cage-type structure;

Bb′ is an amino acid or amino acid analogue or derivative or a structural and/or functional analogue thereof, that comprises one or more guanyl group(s) and/or amidino group(s) and/or its/their analogue(s) and/or derivative(s) and/or structural and/or functional equivalent(s) and/or one or more group(s) that comprise(s) at least two nitrogen atoms each and has/have or can gain a delocalized positive charge;

Cc′ is an amino acid or amino acid analogue or derivative or a structural and/or functional analogue thereof that comprises: one or more side-chain carboxyl group(s) and/or esterified carboxyl group(s) and/or ketoxime and/or aldoxime and/or hydroxamic acid group(s) and/or ketone- and/or aldehyde-carbonyl(s).

and/or Dd-Ee-Ff is one or more of any salt(s), ester(s), amide(s), hydrazide(s), *N*-substituted amide(s), *N*-substituted hydrazide(s), hydroxamic acid derivative(s), any decarboxylated analogue(s), *N*-substituted derivative(s), other related derivative(s), other related analogue(s), and/or any combination(s) of any of such salt, derivative and/or analogue types, of Dd-Ee-Ff as defined above.

174. The use according to claim 173, wherein said Dd-Ee-Ff exhibit(s) selective binding to one or more type(s) of: tumors and/or cancer(s) and/or tumor cells and/or cancer cells and/or malignant cells and/or transformed cells and/or tumor tissues and/or cancer tissues and/or malignant tissues and/or transformed tissues and/or leukemia cells and/or malignant blood cells and/or tranformed blood cells and/or related cells and/or tissues and/or tumor endothelium and/or activated endothelium and/or angiogenic endothelium and/or tumor-endothelium cells and/or activated-endothelium cells and/or angiogenic endothelium cells, and/or their like.

175. The use according to claim 173 or claim 174, wherein said Dd-Ee-Ff exhibit(s) selective binding to one or more type(s) of: tumors and/or cancer(s) and/or tumor cells and/or cancer cells and/or malignant cells and/or transformed cells and/or tumor tissues

and/or cancer tissues and/or malignant tissues and/or transformed tissues and/or leukemia cells and/or malignant blood cells and/or transformed blood cells and/or related cells and/or tissues and/or tumor endothelium and/or activated endothelium and/or angiogenic endothelium and/or tumor-endothelium cells and/or activated-endothelium cells and/or angiogenic endothelium cells, and/or their like, *in vivo* and/or *in vitro* and/or *ex vivo* and/or *in situ*.

176. The use according to any one of the previous claims, wherein said Dd-Ee-Ff exhibit(s) selective binding to one or more type(s) of: tumors and/or cancer(s) and/or tumor cells and/or cancer cells and/or malignant cells and/or transformed cells and/or tumor tissues and/or cancer tissues and/or malignant tissues and/or transformed tissues and/or leukemia cells and/or malignant blood cells and/or tranformed blood cells and/or related cells and/or tissues and/or tumor endothelium and/or activated endothelium and/or angiogenic endothelium and/or tumor-endothelium cells and/or activated-endothelium cells and/or angiogenic endothelium cells, and/or their like, *in vivo*.

177. The use according to any one of the previous claims, wherein said Dd-Ee-Ff exhibit(s) selective binding to one or more type(s) of: tumors and/or cancer(s) and/or tumor cells and/or cancer cells and/or malignant cells and/or transformed cells and/or tumor tissues and/or cancer tissues and/or malignant tissues and/or transformed tissues and/or leukemia cells and/or malignant blood cells and/or transformed blood cells and/or related cells and/or tissues and/or tumor endothelium and/or activated endothelium and/or angiogenic endothelium and/or tumor-endothelium cells and/or activated-endothelium cells and/or angiogenic endothelium cells, and/or their like, *in vitro* and/or *ex vivo*.

178. The use according to any one of the previous claims, c h a r a c t e r i z e d in that said Dd-Ee-Ff is/are capable of binding to one or more type(s) of: primary tumors and/or cancers, and/or tumor/cancer endothelium, and/or tumor/cancer metastases, and/or residive/residual tumors and/or cancers, and/or recurred/recurrent/relapsed tumors and/or cancers, and/or tumor cells; *in vivo* and/or *in vitro* and/or *ex vivo* and/or *in situ*.

Abstract

This invention relates to novel tumor targeting agents, targeting units and motifs, as well as peptides and analogues thereof, and to a variety of compounds and pharmaceutical and diagnostic compositions. The targeting agents typically comprise one or more motif(s) Dd-Ee-Ff, wherein Dd, Ee and Ff may be, for example, various amino acid(s) and/or their analogue(s). This invention relates also to diagnostic and therapeutic methods, and uses of the substances disclosed.